

Thiamethoxam-Induced Subclinical Onychomadesis

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Established Facts

- Various chemicals for household use can cause changes to the nail unit including onycholysis, crumbling of the nail plate, etc.
- Bacterial and fungal infections can occur in a damaged nail unit and worsen prognosis.

Novel Insights

- Subclinical onychomadesis, which progressed to manifest onychomadesis, was observed in our patient following use of thiamethoxam, a broad-spectrum systemic insecticide for use on plants.
- Safety data for thiamethoxam lacks mention of such adverse effects on nails, stating that animal studies have not demonstrated any such effect.
- Management includes long-term treatment of secondary bacterial and fungal infections that arise in such a damaged nail unit.

Keywords

Subclinical onychomadesis · Thiamethoxam · Chloronychia · Irritant contact dermatitis

Abstract

Introduction: Irritant contact dermatitis affecting the nail unit may lead to nail matrix damage and onychomadesis, which may initially be subclinical, becoming overt later. We describe a patient who developed these changes after using a chemical pesticide. **Case Presentation:** A 52-year-old woman presented with discoloration of the nails of both

hands of two days' duration, associated with mild digital pain. She had used an over-the-counter insecticide product containing thiamethoxam (a broad-spectrum systemic insecticide) for her houseplants, preceding the nail changes. Examination revealed onycholysis and subclinical onychomadesis involving multiple fingernails as well as toenails. Onychoscopic examination showed proximal nail plate separation with an erythematous regular border. Histopathology showed an essentially normal nail plate with spongiosis, epidermal cell necrosis, and hypergranulosis. However, there was no evidence of bacterial or fungal infection, and dermal inflammation was mild. The patient was diagnosed

with thiamethoxam-induced irritant dermatitis with subclinical onychomadesis and was advised to take general precautions with avoidance of any further contact with the insecticide. She was managed with topical steroids and emollient; however, on follow-up, she developed green nails, with progression to overt onychomadesis in some nails. Additionally, onychomycosis was observed in few nails in the long-term, which needed to be treated. **Conclusion:** Thiamethoxam is an over-the-counter broad-spectrum insecticide used for houseplants, but its safety data does not mention acute adverse effects on nails, which was a novel finding in our patient. The safety data does mention the use of gloves for preparing and administering the product. Secondary bacterial and fungal infections, which can occur after the initial insult, further worsen the prognosis.

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Introduction/Literature Review

The nail unit, just like the skin, is susceptible to damage from chemical agents which disrupt the lipid barrier and cause protein denaturation. If the nail matrix is affected, cellular damage may be severe enough to cause a temporary cessation of germinative activity, leading to arrested nail growth. This manifests as onychomadesis or proximal separation of the nail plate from the matrix. We present a case where progression from subclinical to manifest onychomadesis was observed following usage of thiamethoxam, an over-the-counter insecticide. The long-term management of ensuing complications is also described.

Case Report

A 53-year-old woman presented with white discoloration of multiple fingernails and both great toenails, noticed about two weeks ago, accompanied by mild pain in the digital tips. She was otherwise healthy, had no skin lesions, fungal infections, oral ul-

cers, or chronic diseases, was not on any drug therapy, and had no acute illness in the recent past. On further probing, she revealed that she had used an over-the-counter insecticide containing thiamethoxam (25% w/w) for her houseplants a few days preceding the onset of the nail changes.

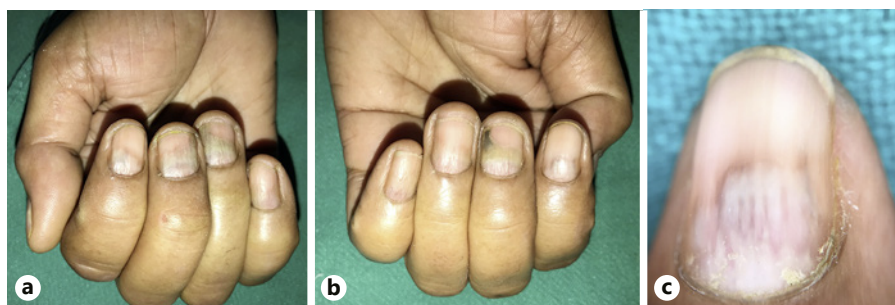
On examination, onychomadesis involving proximal one-third to half of all fingernails was observed. Both great toes had onycholysis. However, the nail plate was still attached and no shedding had occurred (Fig. 1a, b). Onychoscopic examination (Dermlite DL4 ×10) showed well-demarcated onychomadesis with a regular border and erythema distal to it (Fig. 1c). Lamellar splitting (onychoschizia) was also observed at the proximal end of the nail plate in few nails. Direct microscopic examination of the nail clipping with 10% potassium hydroxide (KOH) preparation did not reveal any fungal hyphae or yeasts. Nail biopsy (both nail bed and nail matrix biopsy) revealed the presence of a distinct granular layer, marked spongiosis in the stratum spinosum, and numerous necrotic keratinocytes (Fig. 2). Periodic acid-Schiff stain preparation did not reveal any fungal elements.

Based on the findings, a diagnosis of thiamethoxam-induced irritant contact dermatitis with subclinical onychomadesis was entertained. The patient was prescribed an oral anti-inflammatory agent (ibuprofen) and topical steroid cream and emollients for application over the nail folds. She was also advised to keep the nails dry, avoid contact with detergents or other household chemicals, and use gloves. Nevertheless, 4 weeks later, she presented with green nails (chloronychia) (Fig. 3a) with onychoscopy revealing chloronychia, longitudinal splitting of the nail plate, and normal nail plate emerging proximally (Fig. 3b). It was treated with topical tobramycin solution (0.3%) with the continuation of precautionary measures. Later evolution showed manifest onychomadesis with shedding of affected nail plates by 2 months. This was accompanied by onychomycosis as diagnosed on direct microscopic examination, by 4 months (Fig. 4a, b). She was started on oral fluconazole with topical ciclopirox nail lacquer, with marked improvement (Fig. 5a, b).

Discussion

Samman defined onychomadesis as nail loss due to loosening from the base [1]. It involves separation of the nail plate from the nail matrix with persistent attachment to the nail bed in initial stages, often culminating with complete nail plate shedding. Owing to the slow rate of

Fig. 1. a–c Subclinical onychomadesis involving the proximal part of multiple nails. **a, b** There is erythema of the nail bed, but the surrounding skin is normal in appearance. **c** Onychoscopy (Dermlite DL4 ×10 polarized image) showing proximal leukonychia with well-defined border, showing distal erythema and hyperpigmentation.



nail growth, the process may remain subclinical, with a lag time before clinical manifestation. Onychomadesis has been reported secondary to numerous causes (Table 1).

Alkalis, acids, alkaline-chlorine containing compounds, and detergents can affect a number of changes in the nail unit including, but not limited to, onycholysis, softening and crumbling of the nail plate, discoloration of the nail plate, erosion, ulceration and bleeding from the nail unit, acute onychia, paronychia, and pain in the nails [13].

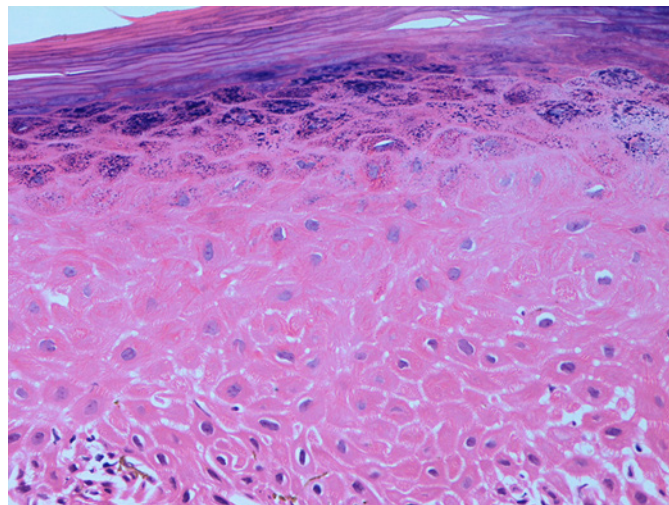


Fig. 2. Photomicrograph of nail biopsy specimen showing orthokeratotic nail plate, with underlying hypergranulosis and marked spongiosis. Basal layer necrotic keratinocytes can be seen (H&E, $\times 400$).

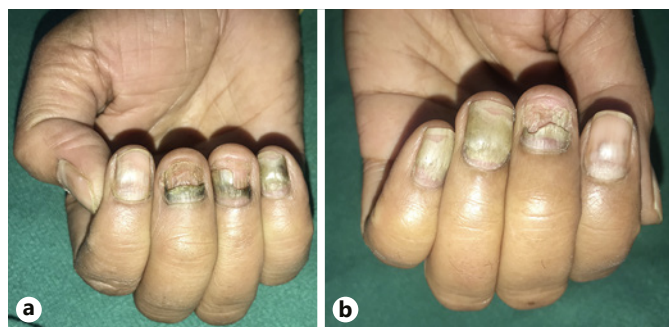


Fig. 3. a, b At one month. **a** Chloronychia involving two nails. **b** Onychoscopy (Dermlite DL4 $\times 10$ polarised image) showing leukonychia involving a large part of the nail. Intervening areas of bright green-black discoloration fading to yellow towards the periphery, suggestive of chloronychia is seen. Artefacts due to ink seen on the surface of the nail plate.

Thiamethoxam is a broad-spectrum neonicotinoid insecticide, belonging to the organochlorine group of compounds, and has a thiazole ring in its structure [14]. Organochlorine compounds such as dichlorodiphenyl-dichloroethylene are known to cause dermatitis in human skin [15]. As per the safety data available, various concentrations of thiamethoxam applied on clipped skin of rats under occlusion have not shown any signs of local irritation [14]. However, in-vitro studies on H9c2 cardiomyoblasts and in-vivo studies on rat models have

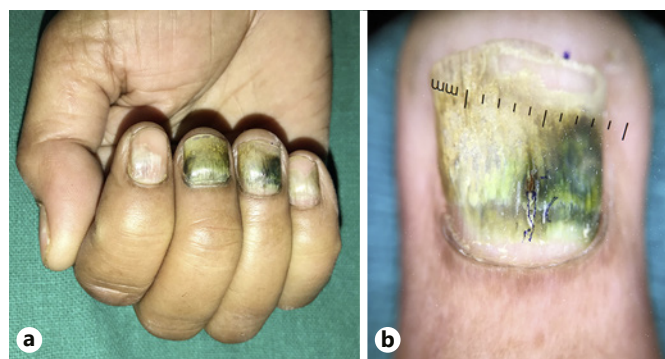


Fig. 4. a, b At two months, significant clearing of chloronychia. However, partial nail loss is noted in three of the nails, which were most affected by chloronychia. The direct microscopic examination of nail plate clippings and subungual debris subsequently showed the presence of fungal elements and patient was started on antifungal therapy.

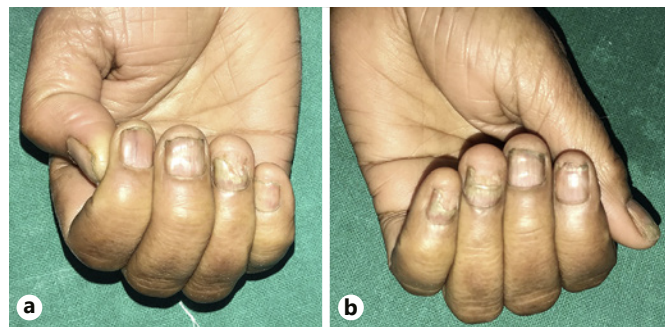


Fig. 5. a, b At 6 months, marked improvement in the nails that had been earlier shed.

Table 1. Causes of onychomadesis described in the literature [1–12]

Infections	Hand, foot, and mouth disease [2] Varicella [3] Onychomycosis (<i>Candida albicans</i> , dermatophytes) [1] Paronychia [4]
Major medical illness	Systemic bacterial infections, meningitis, pneumonia [1] Kawasaki disease [3] Major depressive disorder [3] Stevens Johnson syndrome/toxic epidermal necrolysis [3] COVID-19 [5] Nutritional deficiency [6] Cutaneous leucocytic vasculitis [7]
Inflammatory disease of the nail unit	Nail lichen planus [8] Nail psoriasis [9] Periungual dermatitis [10]
Autoimmune diseases	Pemphigus vulgaris [3] Alopecia areata [11]
Drugs	Chemotherapeutic cytotoxic agents: capecitabine, adriamycin [3] Anticonvulsants: carbamazepine, valproic acid [3] Azithromycin [3] Retinoids [3] Lithium [3]
Trauma	Acute trauma [10] Congenital malalignment of great toe [12]
Idiopathic	Familial (autosomal dominant) onychomadesis [3] Idiopathic sporadic onychomadesis [3]

demonstrated significant cardiotoxicity with damage to cellular lipids and myocyte necrosis [16]. No specific effects on the nail unit have been described, and safety data for commercially available formulations also does not mention any effects. It is commercially available as a crystalline powder, to be reconstituted by dissolving in water and sprayed onto plants. The use of chemical-resistant gloves and footwear along with thorough washing with soap and water after handling is advised [14]. Our patient did not use protective gloves or footwear while reconstituting or using the product. Systemic absorption, if any, could not be estimated. The side-effects observed on the digital tips could have resulted from topical penetration or even systemic absorption. Nevertheless, they have not been previously reported to the best of our knowledge. This report can serve to sensitize users to adhere to safety measures.

Onychomadesis can be a predisposing factor for chlo-
ronychia or onychomycosis. An earlier report of *Candida*
onychomycosis developing in a patient with onychoma-
desis following hand, foot, and mouth disease shows ony-

chomadesis as a risk factor [17]. Lack of protection in our patient led to the initial damage to the nail unit with sub-clinical onychomadesis. Secondary bacterial infection soon followed and clinical evidence of onychomycosis was next, which prolonged the treatment duration and worsened the prognosis. We report this case to highlight a hitherto unreported cutaneous side-effect of a commonly used insecticide, if proper precautions are not used.

Statement of Ethics

The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The subject has given her written informed consent to publish the case (including publication of images). Institutional Ethical Review Board approval was not required for this study in accordance with national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare. None of the authors report any form of support and financial involvement. There are no nonfinancial relationships (personal, political, or professional) that may potentially influence the writing of the manuscript. Dr. Chander Grover is a member of the Editorial Board of “Skin Appendage Disorders.”

Author Contributions

Dr. Chander Grover contributed to the concept, definition of intellectual content, data acquisition, and data analysis. Dr. Sushobhan Saha prepared the first draft of manuscript and contributed to the definition of intellectual content. Both the authors did manuscript editing and review. Dr. Chander Grover shall act as guarantor.

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Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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