

Drug eruption-like scabies surrepticius: an uncommonly described variant of scabies appearing in a non-classic clinical presentation

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To the Editor:

I read with interest the excellent letter by Adris et al. describing a 64-year-old man with metastatic melanoma in whom scabies masqueraded as a drug eruption. A salient feature of his clinical presentation was the suspicion of an adverse event not only from the checkpoint inhibitor nivolumab, but also from the targeted therapies dabrafenib and trametinib, resulting in discontinuation of the treatments until the correct diagnosis was established. Also, in addition to presenting with crusted scabies, he also likely had scabies incognito because of the systemic corticosteroids he had received which alleviated his pruritus but not the associated dermatosis [1].

Sarcoptes scabiei is a mite [2]. In humans, infestation of the parasite results in scabies [3]. It is a highly contagious and typically very pruritic skin condition [4]; indeed, scabies has been misdiagnosed as psychogenic pruritus and uremic pruritus [5,6].

Classic scabies presents with lesions, referred to as burrows, that are often found on flexure sites such as the web spaces between fingers and the wrists [3,4]. In addition, the lesions not only have a predilection to appear on the areola and umbilicus, but also can be found on areas covered by the patient's underwear such as the belt line, buttocks, genitalia, and groin [3,7]. Hyperkeratotic subungual lesions may be an unsuspected reservoir for persistent infestation in scabies patients with therapy-resistant or recurrent mite infestation [3,8-10].

The diagnosis of scabies can be definitively established by observing either the mite, its eggs, or its excrement (scybala), [3]. When a suspected lesion has been identified, some of the procedures that can be used include performing a microscopic evaluation of a skin scraping from the lesion, a dermatoscopic examination of the cutaneous lesion, or a biopsy of the lesion for subsequent microscopic examination of the processed tissue specimen [3,4,11]. Recently, criteria that were developed to be used in the research setting to provide either a confirmed or a clinical or a suspected diagnosis of scabies are now being applied in the office setting [11].

However, scabies infestation can be variable in its morphologic appearance and the diagnosis of scabies may not be suspected. Indeed, the nomenclature scabies surrepticius was coined in 2017 to provide a term for the medical lexicon that encompassed all the non-classic clinical presentations associated with this mite [12]. Several subtypes of scabies surrepticius have been described (**Table 1**), [1,3,5,7-10,12-49]; the patient of Adris et al. exemplifies the uncommonly described drug-eruption-like scabies surrepticius subtype [1].

Similar to the patient of Adris et al., to the best of my knowledge, there are 6 other scabies patients who initially had been misdiagnosed as having an adverse drug reaction (**Tables 2, 3**), [1,8,19,24-27]. Four of the reported individuals were identified by

Table 1. Subtypes of *scabies surrepticius*.

Subtype	Reference
Actinic keratosis	[13]
Bullous	[12,14]
Contact dermatitis-like	[15]
Crusted	[1,13,16-19]
Darier disease-like	[20]
Dermatitis-like	[3]
Dermatitis herpetiformis-like	[21]
Dermatomyositis-like	[22]
Dyshidrotic dermatitis-like	[23]
Drug eruption-like	[1,8,19,24-27]
Ecchymoses	[28]
Erythrodermic dermatitis-like	[16,26]
Face	[8,10,18,25,29]
Hidden ^a	[30]
Incognito	[15-17,19,25]
Indeterminate cell histiocytosis-like	[31,32]
Langerhans cell histiocytosis-like	[18,33]
Leukocytoclastic vasculitis ^b	[34-36]
Lichen simplex chronicus-like	[5]
Nail ^c	[8-10]
Nodular ^d	[3,7,10,37]
Palmar and/or plantar lesions ^e	[9,10,14,18,19,27,29,31,38,39]
Pityriasis rosea-like	[40]
Prurigo nodularis	[41]
Psoriasis-like	[9,39,42,43]
Scalp	[10,16-18]
Seborrheic dermatitis-like	[44]
Subcorneal pustular dermatosis-like	[45]
Systemic lupus erythematosus-like	[41,46]
Urticaria-like	[47]
Urticaria pigmentosa-like	[48,49]

^aHidden scabies, also referred to as unrecognized scabies, was described in a woman (following an automobile accident) who presented with an atypical eczema. *Sarcoptes scabiei* DNA was detected in scales from her skin using polymerase chain reaction [30].

^bScabies-associated vasculitis can be a reactive condition to the mite infestation [35,36]. However, in some of the patients with leukocytoclastic vasculitis scabies *surrepticius*, the skin biopsy of the clinical vasculitis lesion demonstrated a mite in the stratum corneum and pathologic changes of vasculitis in the dermis [34,35].

^cNail scabies can be located either within the nail plate (ungual scabies) or beneath the nail plate (subungual scabies).

^dNodular scabies *surrepticius* includes not only scrotal lesions but also lesions on other body locations. The scrotal lesions are commonly reactive and do not contain mites; however, mites have occasionally been observed in scrotal nodules. In contrast, although nodular lesions on other areas of the body may be reactive, mites are often present in non-genital nodules.

^eLesions such as blisters and pustules on the palms and soles are commonly observed in newborns; but pustular lesions have also been in elderly patients.

either “adverse drug reaction” or “drug eruption” in the title of the paper [1,19,25,27]. However, scabies masquerading as an adverse side effect from the medications that the patient was receiving was only mentioned in the case report section for three of the individuals [8,24,26]. Hence, it is possible that there are additional patients with this subtype of scabies *surrepticius* that have been described in the medical literature.

Drug-eruption-like scabies *surrepticius* was observed predominantly in older patients; there were four men and three women. They ranged in age, when diagnosed with scabies, from 34 years old to 85 years old (median, 77 years old) but 6 of the patients were older than 64 years. The men were younger (34 years old to 65 years old; median, 65 years old) than the women (79 years old to 85 years old, median 85 years old) when the diagnosis of scabies was established. The patients were from varying countries around the world.

The mite infestation had been present as briefly as two days to as long as two years (median, four months) before the diagnosis was scabies was determined. All the patients had medical conditions. Indeed, the medications suspected to be causing the suspected adverse drug reaction were agents being used in the acute or chronic treatment of the individual’s medical problems.

Pruritus was present in all the patients with drug-eruption-like scabies *surrepticius* in whom symptoms were described. The morphology of the mite-associated lesions was variable; they included hyperkeratotic lesions, facial swelling, lichenified lesions, nail dystrophy, papules, pustules, and scaly lesions.

In addition to mimicking an adverse reaction to a medication, drug-eruption-like scabies *surrepticius* was most frequently (6 of 7 individuals) observed in patients with crusted scabies; a single person had disseminated papules and excoriations. In addition to initially presenting with classic lesions of scabies in one patient, other clinical variants of scabies *surrepticius* included erythrodermic dermatitis and incognito; the latter patients had been treated with topical corticosteroids. In addition, the face (two

Table 2. Epidemiologic features of patients with drug-eruption-like scabies *surrepticius*.

C	Age (years)	G	Nationality	Duration ^a (months)	Medical conditions	Suspected drugs	Ref
1	34	M	Kosovo	6.67	Acute myelogenous leukemia	Cytarabine Idarubicin	[24]
2	64	M	United States of America	18	Metastatic malignant melanoma	Dabrafenib Nivolumab Trametinib	[1]
3	65	M	Japan	1	Alcohol-related hepatic cirrhosis	Drugs	[25]
4	77	M	England	4.25	Barrett esophagus Congestive heart failure Senile dementia	Bumetamide Captopril Lanzoprazole	[19]
5	79	W	Israel (Moroccan and Jewish descent)	6	Congestive heart failure Myelodysplastic syndrome Thrombocytopenia	Permethrin (topical)	[8]
6	85	W	United States of America	24	Femoral artery embolism	Drugs	[26]
7	85	W	Slovak Republic (Slovakia)	4	Bullous pemphigoid Ischemic heart disease	HCTZ Lacipil	[27]

C, case; G, gender; HCTZ, hydrochlorothiazide; M, man; Ref, reference; W, woman.

^aNumber of months that dermatosis was present prior to establishing the diagnosis of scabies.

patients) and nails (one patient) were scabies *surrepticius*-associated body sites of the mite infestation in two of the patients with drug-eruption-like subtype of scabies *surrepticius*.

The most common location of mite-associated lesions was the hands (5 patients). Three individuals had scabies-related lesions on the extremities [arm (one patient), leg (one patient), and both arm and leg (one patient)] or the torso [trunk (two patients), and back (one patient)]; in addition, three patients had lesions that were either observed to be widespread (two patients) or on their whole body (one patient). Two patients had lesions at each of the following body areas: face, feet, finger webs, genitals or groin, nails, and wrist.

The definitive diagnosis of scabies was established in all the patients by observing either the mite, its eggs, or its excrement (scybala) during a microscopic evaluation of a skin scraping from a lesion. Three patients also had confirmation of the diagnosis from examination of the processed tissue specimen from a lesion biopsy. However, the biopsy evaluation was consistent with a drug eruption and negative for scabies mite, eggs, or feces from three of the patients with drug-eruption-like scabies *surrepticius*.

Four of the patients with drug-eruption-like scabies *surrepticius* were only treated with topical therapies: benzyl benzoate, crotamiton, lindane, permethrin, precipitated sulfur, and/or salicylic acid. The other three patients were treated not only with one or more topical agents, but also oral ivermectin. There was complete and sustained resolution of the scabies infestation in all 6 of the patients in whom the response to treatment was described; the result of treating the 65-year-old man with 10% crotamiton ointment was not reported.

The 34-year-old man with acute myelogenous leukemia developed fungal (*Aspergillus fumigatus*) and bacterial (*Stenotrophomonas maltophilia*) infections of his lungs. The infections were attributed to chemotherapy-induced neutropenia and not consider to be a complication of his mite infestation. In addition to resection of the pulmonary fungal infiltrates from both lungs, he received systemic antifungal and antibiotic therapy; both infections cleared as his neutrophil count recovered [24].

Three of the drug-eruption-like scabies *surrepticius* patients had mite infestation-related *Staphylococcus aureus* infection or colonization. The 65-year-old man died secondary to septic shock due to *Staphylococcus aureus* [25]. The 77-year-old man's

Table 3. Clinical characteristics of patients with drug-eruption-like scabies *surrepticius*.

C	Itch	Lesion morph	Scabies clinical variant	Lesion location	Scabies dx	Treatment	RTT	Ref
1	Yes	Papule	Disseminated	Buttocks, finger webs, genitals, trunk, wrists	Bx: - SS: +	Lindane QD ×3, repeat s/p 1 wk Ivermectin 12 mg × 1 dose Two wks later, repeat both ×1	Res	[24]
2	Yes	Papule Pustule	Crusted	Buttocks, extremities, finger webs, groin, hands, trunk, wrist	Bx: - SS: +	Ivermectin Permethrin	Res	[1]
3	Yes	Hyperk Scaly	Crusted Face Incognito	Face, whole body	SS: +	10% crotamiton ointment	NS	[25]
4	Yes	Hyperk Lichen Scaly	Crusted Incognito	Feet, hands, widespread	Bx: - SS: +	Twice to body: benzyl benzoate Permethrin to head & neck	Res	[19]
5	NS	Facial swelling Nail dys Scaly	Classic Crusted Face Nail	Face, hands, nails	Bx: + SS: +	Ivermectin: day 1,2,8,9,22,29 Nail removal: 30% sal acid Permethrin × 1 10% sulfur ointment	Res	[8]
6	Yes	Scaly	Crusted Erythro dermatitis	Feet, hands, widespread	Bx: + SS: +	Lindane (scalp to toes) on days 1,2,4,5 Fluocin 0.025% ointment BID	Res	[26]
7	Yes	Hyperk	Crusted Erythro dermatitis	Arms, back, hands, thigh, trunk	Bx: + SS: +	10% ppt sulfur & 10% sal acid, both in vasoline QD × 6	Res	[27]

BID, twice daily; Bx, biopsy; C, case; dx, diagnosis; Dissem, disseminated; dys, dystrophy, erythro, erythrodermic; Fluocin, fluocinolone acetonide; Hyperk, hyperkeratotic; morph, morphology; NS, not stated; ppt, precipitated; QD, daily; Ref, reference; Res, resolved; RTT, response to treatment; sal, salicylic; SS, skin scraping; s/p, after; wk, week; wks, weeks; +, positive observation of mite, eggs, or scybala; -, no observation of mite, eggs, or scybala; % percent; &, and.

skin lesions became infected and he required hospitalization to treat his Staphylococcal septicemia; he was discharged after three days of antibiotic treatment and resolution of the infection [19].

Extensive bacterial colonization of the scabies burrows from the 85-year-old woman were demonstrated on scanning electron microscopy. Many cocci were also observed on smears of the mite scybala; bacterial culture of the mite feces grew *Staphylococcus aureus*. She was orally treated with 250 milligrams of erythromycin, four times daily, for 10 days [26].

Similar to the patients with drug-eruption-like scabies *surrepticius* who developed *Staphylococcus aureus* infection or colonization, the clinical presentation of scabies can be altered by the

concurrent presence of bacterial or viral infection. The morbidity of the mite infestation can be significantly increased when secondary infection of the lesions by either *Staphylococcus aureus* or *Streptococcus pyogenes* occurs [4,10,14,19,25,26,50]. Scabies herpeticum—referring to mite-related lesions that have become infected by herpes simplex virus—can appear as superficial ulcers. This atypical, albeit less commonly reported, appearance of scabies may delay the diagnosis and subsequent treatment of the mite infestation [51,52].

Hence, similar to the patient of Adris et al. [1], the diagnosis of scabies *surrepticius* can be difficult to confirm, especially when the associated clinical history and morphologic appearance of the lesions are suggestive of another condition or the lesions are infected with a bacterial or a viral pathogen [53].

Indeed, a non-diagnostic skin biopsy can be misleading, result in treatment that further alters the lesion presentation, and delays the correct diagnosis [1,5,19,24]. Therefore, in a patient with a sustained or progressive skin condition—particularly if it is pruritic—that has not responded to therapeutic interventions, the possibility of scabies should be entertained and additional diagnostic evaluation considered [1,3].

In addition, with regard to establishing a diagnosis of scabies, often other people who have been in close contact with the patient shall also have symptoms (such as itching) and mite-associated lesions [3,5,8,14,19,26,37]. This is especially important for individuals with a prolonged duration of their undiagnosed or misdiagnosed condition. Therefore, obtaining additional history from the patient or family members or caregivers is crucial [53]. Also, it may be appropriate to empirically treat these individuals for scabies, even if they are asymptomatic [3,10].

In conclusion, the prompt diagnosis of scabies is important not only for the treatment of the affected individual but also to prevent the potential transmission of the contagious mite to people with whom the patient contacts. When a person has classic symptoms (such as pruritus that is more

severe in the evening) and lesions suggestive of a mite infestation (such as burrows that are located on flexor sites), the clinician can use objective evidence to provide a confirmed diagnosis or subjective observations to fulfill criteria of either a clinical or suspected diagnosis of scabies. However, the clinician may not suspect the possibility of a mite-associated dermatosis in an individual who has scabies surrepticius and presents with non-classic manifestations of the condition. Some of the variants of scabies surrepticius—such as crusted, incognito, and nodular types—are more common whereas other subtypes with bullae, nail involvement (either within the nail plate or subungual), or involvement of the face, palms, scalp, and soles are observed less frequently. Scabies masquerading as an adverse effect to a medication has seldom been described. However, the possibility of drug-eruption-like scabies surrepticius should be entertained in a patient with a suspected medication reaction that persists as a pruritic dermatosis after discontinuation of the drug and has clinical lesions suggestive of crusted scabies.

Potential conflicts of interest

Dr. Cohen is a consultant for ParaPRO and declares no conflicts of interest.

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