

Mask-induced Koebner phenomenon and its clinical phenotypes: A multicenter, real-life study focusing on 873 dermatological consultations during COVID-19 pandemics

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Abstract

During COVID-19 pandemic, wearing masks for prevention became mandatory but evidence suggest that is also detrimental for skin. Although facial dermatoses due to masks increase in both healthcare workers and general population, a pathogenetic hypothesis remains still elusive. We aimed to evaluate the prevalence of dermatological consultations due to Koebner triggered dermatoses In this prospective, multicenter, real life study carried out in Italy from March 11th to December 11th 2020 during COVID-19 pandemics, dermatological consultations (in-person and telemedicine) to study the prevalence of Koebner (KB) phenomenon due to masks were evaluated. Boyd and Nelder classification was adopted for Koebner phenomenon and Bizzozero's for KB intensity. A total of 229/873 (26.2%) dermatological consultations were KB triggered dermatoses and lesions were located in mask-covered ear area (76 [33.2%]), malar area (73 [31.8%]), perioral area (53 [23.1%]), and nose (27 [11.8%]). The first KB category grouped 142 patients (psoriasis, vitiligo, maskne, and mask rosacea), the second one 24 (warts, molluscum contagiosum, and impetigo), the third one 46 (atopic dermatitis), and the fourth one 17 (eczema). Among previously KB negative psoriatic patients that became KB positive, 9/13 (69.2%) had discontinued or modified the prescribed antipsoriatic treatment. Mask-related Koebner phenomenon is an important clinical sign to orient clinician's therapeutic protocols during COVID-19 pandemic, especially in patients with psoriasis.

KEYWORDS

COVID-19, facial dermatoses, Koebner clinical phenotypes, Koebner mask induced, personal protective equipment, psoriasis, surgical masks, telemedicine

Giovanni Damiani and Laura Cristina Gironi contributed equally to this study.

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1 | INTRODUCTION

During COVID-19 pandemics, overwhelmed healthcare systems promoted self-preventive strategies to avoid SARS-CoV-2 infection, spacing from lockdown to mask wearing.¹⁻³ Dermatology departments worldwide reprioritized visits and improved telemedicine consultation in both primary and follow up visits.⁴⁻⁶ Wearing masks became mandatory initially for healthcare workers and after also for civilians,⁷ changing skin exposure and the whole facial exposome.⁸ Despite hypotheses multiplied, the pathogenetic mechanism of mask-induced dermatoses remains elusive.

Masks short-term and long-term wearing for preventive exigencies are also changing the dermato-epidemiology,^{9,10} forcing dermatologists to integrate guidelines based on evidence.¹¹

Recently, Mutalik et al described a Koebner phenomenon (KB) due to mask in a 74 years old patient with psoriasis, rising the possibility that mask via KB may worsen preexisting facial dermatoses.¹²

Thus, we decided to perform a study focusing on mask-induced Koebner phenomenon on patients referred to dermatology during COVID-19 pandemic.

2 | MATERIALS AND METHODS

2.1 | Study design

This is a prospective, multicenter, real life study that involved three primary referral dermatological centers in Italy (IRCCS Istituto Ortopedico Galeazzi, IRCCS San Gallicano and Maggiore della Carità) carried out from March 11th to December 11th 2020 during COVID-19 pandemics.

Dermatological consultations (in-person and telemedicine) were recorded to understand the role of masks in triggering Koebner phenomenon.

Telemedicine video calls were performed with different platforms (FaceTime, WhatsApp, Skype, Zoom, or Go-to-Meeting), depending from patients preferences, and lasted 15 minutes.

2.2 | Dermatological assessment

To assess Koebner phenomenon we adopted Boyd and Nelder's classification,¹² summarized in Table 1. In line with Bizzozzero et al,¹⁴ KB intensity was rated as "maximal" for lesions developed across the entire mask covered area, "minimal" for lesions developed in focal areas covered by mask, "abortive" for lesions vanishing spontaneously in 12-20 days, and "none" for absence of lesions.

Koebner phenomenon was clinically and dermatoscopically differentiated from "patergy" since new lesions appearing on unaffected skin were specific of facial preexistent dermatoses, whilst medical history contributed to differentiate KB from "reverse KB" (existing lesions that disappear after trauma) and "Wolf's isotopic response" (lesions appear after a trauma and anticipate the dermatosis occurrence).¹⁵

Coherently with the nosologic definition, we defined maskne/mask rosacea as koebnerized dermatoses only if the acne/rosacea worsened in areas mask-covered after regular mask wearing.¹⁶ Patients with rosacea underwent patch tests¹⁷ to rule out a possible concurrent allergic contact dermatitis due to mask release of formaldehyde.¹⁸

Demographics (age, gender) and clinical data (dermatoses severity, medical history, and drug intakes) were carefully recorded together with mask related data (prevalent mask wearing model and daily mask wearing duration).

Dermatoses severity indexes adopted in this study are: Psoriasis Area Severity Index (PASI) for psoriasis,¹⁹ Vitiligo Area Scoring Index (VASI) for vitiligo patients,²⁰ Global Acne Grading Scale (GAGS) for maskne patients,²¹ Investigator Global Assessment (IGA) for mask rosacea, and impetigo patients,²² Eczema Area and Severity Index (EASI) for patients with both atopic dermatitis and eczema.²³

2.3 | Statistics

Normal distribution for each variable was investigated by performing the Kolmogorov-Smirnov test. Data were reported as mean \pm SD or median

TABLE 1 Boyd and Nelder classification of Koebner phenomenon

Number	Boyd and Nelder category	Clinical description	Phenotype related dermatoses
I	True Koebnerization	Lesions are clinically similar to the underlying primary dermatological disease and appear in a location not previously involved after a reproducible trigger.	Psoriasis, vitiligo, lichen planus
II	Pseudo Koebnerization	Traumatic triggers (ie, scratching) allow microbes to penetrate the cutaneous barrier and cause lesions	Warts, molluscum contagiosum, impetigo
III	Occasional koebnerization	Traumatic triggers, not fully reproducible, elicit lesions	Lichen sclerosus, erythema multiforme, Hailey-Hailey disease, darier disease, perforating folliculitis, pityriasis rubra pilaris, atopic dermatitis, bullous pemphigoids
IV	Poor or questionable trauma-induced processes	The relationship between triggering trauma and lesions is pathogenetically plausible	Lichen nitidus, eczema, pemphigus vulgaris, porokeratosis of mirabelli, discoid lupus

[interquartile interval] as well as percentage and all the analyses were conducted by using the MedCalc Statistical Software version v19.0.3 (MedCalc Software bvba, Ostend, Belgium).

3 | RESULTS

3.1 | Dermatological consultation data

During the study we recorded a total of 873 dermatological consultations, in which 257 (29.4%) performed in telemedicine (89 with WhatsApp, 73 with FaceTime, 56 with Go-to-Meeting, 15 with Skype, and 24 with Zoom). Mask-related consultations were 302 (34.6%) comprehensive of 229 (26.2%) that were classified as KB triggered dermatoses (Table 2). KB triggered dermatoses were mainly diagnosed with in-person consultations (203 vs 26).

Lesions were located in mask-covered ear area (76 [33.2%]), malar area (73 [31.8%]), perioral area (53 [23.1%]), and nose (27 [11.8%]) (Figure 1). Dermatological consultations performed on healthcare workers for KB triggered dermatoses were 72 (31.4%).

3.2 | Boyd and Nelder I category or “true koebnerization”

This category is the largest one and grouped 142 (M/F ratio = 1/2.8) patients, namely 37 with psoriasis, 14 with vitiligo, 65 with maskne, and 26 with rosacea.

Patients with psoriasis (12 [32.4%] had also a diagnosis of psoriatic arthritis) displayed a median PASI of 5.3²⁻¹⁴ and before mask use 40% were clinically stable (<10% PASI variation in two consecutive visits). Thirty patients underwent systemic antipsoriatic therapies (15 secukinumab, 8 ixekizumab, 7 ustekinumab, 4 adalimumab, 2 apremilast, and 1 etanercept) and 13 were previously Koebner negative (no previous KB episodes). Interestingly, 9/13 (69.2%) declared to discontinue or modify anti-psoriatic treatments.

Patients with vitiligo displayed a median VASI of 8.1⁴⁻¹⁴ and were previously stable under topical treatments (N = 10) and NB-UVB (N = 4). They present with active disease and increased spread of perioral (N = 13) and chin (N = 1) hypopigmented patches. All patients were Koebner positive previously.

Patients with maskne displayed a median GAGS of 11.6⁸⁻¹⁴ with a higher concentration of comedonic and pustular new lesions in

TABLE 2 Demographics and clinical data of Koebner phenotypes mask related in our cohort

Boyd and Nelder' category	Facial dermatoses (N)	Koebner response intensity (N [%])	Age (median [IQR], years)	Male (N [%])	Type of mask (N [%]) ^a	Daily mask wearing (median [IQR], hours)
I	Psoriasis: 37	Maximal: 2 (5.4) Minimal: 35 (94.6) Abortive: 0 (0)	43 [22-56]	13 (35.1)	SM: 16 (43.2) N95: 7 (18.9) Community mask: 14 (37.8)	8 [6-12]
	Vitiligo: 14	Maximal: 1 (7.1) Minimal: 13 (92.9) Abortive: 0 (0)	35 [20-47]	3 (21.4)	SM: 5 (35.7) N95: 0 (0) Community mask: 9 (64.3)	7 [6-9]
	Maskne: 65	Maximal: 13 (20.0) Minimal: 52 (80.0) Abortive: 0 (0)	31 [20-37]	17 (26.2)	SM: 46 (70.8) N95: 11 (16.9) Community mask: 8 (12.3)	7 [5-8]
	Mask Rosacea: 26	Maximal: 2 (7.7) Minimal: 24 (92.3) Abortive: 0 (0)	56 [41-66]	4 (15.4)	SM: 15 (57.7) N95: 3 (11.5) Community mask: 8 (30.8)	6 [5-8]
II	Warts: 11	Maximal: 0 (0) Minimal: 11 (100.0) Abortive: 0 (0)	14 [8-21]	5 (45.5)	SM: 9 (81.8) N95: 0 (0) Community mask: 2 (18.2)	7 [5-8]
	Molluscum contagiosum: 4	Maximal: 0 (0) Minimal: 4 (100.0) Abortive: 0 (0)	7 [3-12]	2 (50.0)	SM: 0 (0) N95: 0 (0) Community mask: 4 (100.0)	4 [3-6]
	Impetigo: 9	Maximal: 0 (0) Minimal: 9 (100.0) Abortive: 0 (0)	8 [2-14]	3 (33.3)	SM: 2 (22.2) N95: 4 (44.4) Community mask: 3 (33.3)	5 [3-7]
III	Atopic Dermatitis: 46	Maximal: 5 (10.9) Minimal: 41 (89.1) Abortive: 0 (0)	29 [16-43]	13 (28.3)	SM: 15 (32.6) N95: 13 (28.3) Community mask: 18 (39.1)	7 [5-8]
IV	Eczema: 17	Maximal: 1 (5.9) Minimal: 14 (82.4) Abortive: 2 (11.8)	62 [48-73]	9 (52.9)	SM: 9 (52.9) N95: 3 (17.6) Community mask: 5 (29.4)	6 [5-8]

Abbreviations: IQR, interquartile interval; SM, surgical mask.

^aThis parameter refers to the main type of mask wore by the examined patient.



FIGURE 1 Mask-related Koebner phenomenon in psoriatic patients. A, Linear, erythematous and desquamating lesions on supraauricular area of the left ear under the mask laces. B, Diffuse erythematous and desquamating lesions on pre-auricular, mandibular and malar areas covered by mask. C, Severe erythema and desquamation in retroauricular area in contact with mask laces. D, Linear, desquamating plaques on cefalo-auricular fold in contact with mask laces

mask-covered areas. They were treating their lesions with benzoyl peroxide (N = 4), tretinoin gel (N = 10), oral antibiotics (N = 37), oral spironolactone (N = 11), and oral isotretinoin (N = 3).

Patients with mask-rosacea had a median IGA of 2¹⁻³ and displayed papulo-pustular (N = 18) and erythematotelangiectatic phenotypes (N = 8) with an increase in erythema, papules, and pustules in mask-covered areas. They were treating rosacea with topical metronidazole (N = 17), topical ivermectin (N = 3), and oral antibiotics (N = 6).

3.3 | Boyd and Nelder II category or “pseudo koebnerization”

This category mainly include pediatric patients that spread infectious dermatoses (Warts = 11, Molluscum contagiosum = 4, and

Impetigo = 9) on mask-covered areas. Patients experienced itch under mask and they scratch the area interrupting the cutaneous barrier and seeding etiologic microbes. Lesions concentrated on nose and upper lip.

3.4 | Boyd and Nelder III category or “occasional koebnerization”

This category encloses 46 patients with atopic dermatitis that experience a flare mainly concentrated in mask-covered areas. Patients displayed a median EASI of 17 (7-53) and were treated with topical corticosteroids (N = 28), topical calcineurin inhibitors (N = 11), and dupilumab (N = 7). Erythematous and eczematous lesions were mainly concentrated in nasal and malar area.

3.5 | Boyd and Nelder IV category or “poor or questionable trauma-induced processes”

This category contains patients with facial, nonatopic eczema; they are older than other patients and present eczematous lesions located on malar area.

3.6 | Masks type

Since different masks establish a different cutaneous microenvironment we recorded mask types finding that 117 (51.1%) patients wore surgical masks (SM), 71 (31.0%) patients wore community masks, and only 41 (17.9%) patients wore N95 masks. Beside pediatric patients belonging to Boyd and Nelder III category, masks wearing overwent 6 hours/day.

4 | DISCUSSION

Masks during COVID-19 pandemic trigger both de novo dermatoses¹⁰ and also worsen pre-existing ones; mask-covered areas are exposed to proinflammatory microenvironment⁸ capable to cause, in certain patients, Koebner phenomenon.

KB is present in approximately 25%-30% of psoriatic patients and contributes to the development of new lesions in uninvolved skin.²⁴ Its pathogenesis remains elusive, but recently resident mast cells and keratinocytes activation was regarded as potential mechanism. In fact, keratinocytes activated by traumas release IL-33 that activate mast cells, then mast cells via triptase trigger epithelial cells, fibroblasts, and neutrophils.²⁵ Mast cells together with keratinocytes produce IL-17 leading to a proinflammatory local microenvironment capable to sustain the development of new psoriatic plaques.²⁵ Psoriasis is a chronic, systemic, inflammatory disease, and a growing body of evidence both omics²⁶ and non-omics based²⁷ suggest that uninvolved skin clinically similar but immunologically different from the healthy one.^{26,27} Thus, mask-related mechanic traumas may trigger new psoriatic lesions in 10-14 days also on uninvolved skin that displays a proinflammatory profile.^{26,27}

During COVID-19 pandemic, some psoriatic patients discontinued/modify antipsoriatic prescribed therapies²⁸ due to the supposed higher possibility to get infected by SARSCoV-2.^{29,30} Interestingly, among our psoriatic patients previously Koebner negative, 70% discontinued or even modified the prescribed antipsoriatic therapy, coherently Koebner new positivity could be also regarded as a clinical sign of patient loss of adherence. Likewise, true koebnerization in vitiligo patients suggest higher disease activity and poor treatment response,³¹ so vitiligo patients with mask-related Koebner should be treated with more aggressive treatment protocols.

Maskne (acne due to mask) and mask rosacea are classified as “true Koebner” since our current understanding is that the inflamed pilosebaceous units are further influenced by mask-related

microenvironment and mask-related mechanic traumas, as hypothesized for vitiligo KB mask-related.¹⁶

Masks also cause itch^{32,33} and scratching derived injuries, the exact pseudo Koebner pathogenesis capable to explain KB related impetigo, warts, and molluscum contagiosum.

Third and fourth Boyd and Nelder' categories are communed by the cutaneous barrier defects that further amplify mask-derived inflammation.

Despite its innovative evaluation in assessing Koebner phenomenon due to masks, our study present also the limitation that telemedicine consultations were performed with several video call platforms with a resolution dependent from patient's line and device. Furthermore, due to the limited patients sample for every single dermatosis, it was not possible to evaluate the influence of mask type and donning duration in triggering KB in each dermatosis evaluated.

In conclusion, mask-related Koebner phenomenon is an important clinical sign to orient clinician's therapeutic protocols, especially in patients with psoriasis and vitiligo. Further studies and big data³⁴ are needed to understand in detail the immunological changes induced by masks.

CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Giovanni Damiani, Laura C Gironi, Khalaf Kridin, Alessia Pacifico: Conceptualization; Giovanni Damiani. and Alessia Pacifico: Methodology; Nicola L Bragazzi and Magdalena Spalkowska: Software; Giovanni Damiani, Alessia Pacifico, Alessandra Buja and Pierachille Santus: Validation; Nicola L Bragazzi: Formal analysis; Giovanni Damiani, Laura C Gironi, Alessia Pacifico, Khalaf Kridin. and Magdalena Spalkowska: Investigation; Giovanni Damiani, Alessandra Buja, Pierachille Santus and Paolo DM Pigatto: Resources; Alessandra Buja and Pierachille Santus: Data curation; Giovanni Damiani, Laura C Gironi, Alessia Pacifico, Khalaf Kridin, and Pierachille Santus: Writing—Original Draft; Giovanni Damiani, Laura C Gironi, Khalaf Kridin, Alessia Pacifico, Alessandra Buja, Nicola L Bragazzi, Magdalena Spalkowska, Paolo DM Pigatto, Pierachille Santus, and Pierachille Santus: Writing—Review & Editing; Khalaf Kridin, Nicola L Bragazzi and Pierachille Santus: Visualization; Pierachille Santus, Alessandra Buja, and Paolo DM Pigatto: Supervision; Giovanni Damiani, Laura C Gironi and Paolo DM Pigatto: Project Administration.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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