

Chilblain-like lesions (COVID-19 toes) have the same impact on family members than psoriasis systemically treated: insights from a case-control study targeting the pediatric population

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Abstract. – OBJECTIVE: COVID-19 toes represent the main dermatological COVID-19 cutaneous manifestation in pediatric patients. Its diagnosis exposes the whole family to social stigma and this aspect was not previously evaluated.

PATIENTS AND METHODS: This was a multicenter, case-control, observational study that compared the family impact of COVID-19 toes vs. psoriasis (PsO). We enrolled 46 pediatric patients (23 with psoriasis and 23 with COVID-19 toes, age and gender matched) and their parents/caregivers that had to fill the Dermatitis Family Impact (DFI) questionnaire.

RESULTS: DFI index did not differ significantly between both subgroups ($p=0.48$), and in psoriatic patients did not correlate with both Psoriasis Area Severity Index (PASI) ($p=0.59$) and itch-VAS ($p=0.16$).

CONCLUSIONS: COVID-19 toes, a transitory dermatosis, exerted a similar impact/perturbation on family dynamics than PsO, a well-known stigmatizing, chronic inflammatory dermatosis.

Key Words:

COVID-19 toes, Chilblain-like lesions, Psoriasis, Pediatrics, Dermatitis family impact.

Introduction

“Chilblain-like lesions” or “COVID-19 toes” or “COVID-19 -related acute acroischemia” represent the first cutaneous manifestation of SARS-CoV-2 characterized in both symptomatic and asymptomatic children during pandemic^{1,2}.

Acral vasculitis starts with 1-2 red round elements on the hands and/or feet progressively increasing in 2-3 days with multifocal, asymmetric polymorphous evolution (erythema and infiltration or erythema, exudation, and hemorrhagic lesions) spontaneously regressing in 12-20 days (Figure 1).

Remarkably, lesions are often reported as itching, burning and painful, sometimes impairing mobility³⁻⁵.

After medical consultation, COVID-19 toes therapeutic management in pediatric patients is mainly performed at home by parents and/or caregivers³. Remarkably, media and dermatological associations worldwide have increased general population awareness of this SARS-CoV-2 cutaneous manifestation for preventive purposes,

but at the same time also increased society stigmatization for COVID-19 toes patients as well as anxiety in their family.

Currently, there is no data present to evaluate COVID-19 toes family impact. Due to this fact, aim of this study was to perform a study by enrolling these types of patients and compare them with a well-known stigmatizing condition, such as psoriasis (PsO).

Materials and Methods

Study Design

This is a multicenter a multicenter, case-control, observational study that involved 6 primary Italian referral centers (IRCCS Istituto Ortopedico Galeazzi, IRCCS San Donato, IRCCS San Gallicano, Maggiore della Carità di Novara, Azienda Ospedaliera Federico II of Napoli, Policlinic consortium hospital-university of Bari) between March and October 2020.

The main focus was pediatric population (<15 years and 11 months) matching cases (COVID-19



Figure 1. COVID-19 related acral manifestations. **A**, Erythematous lesions on fingers. **B**, Erythematous, violaceous, infiltrated lesions involving III and V toes: **C**, Red-violet hemorrhagic elements on the calcaneum. **D**, Round hemorrhagic elements on the lateral plantar.

toes) and controls (Psoriasis) for age, gender, and Dermatitis Family Impact (DFI) questionnaire parent responder characteristics (age and gender). The demographics, clinical and familiar data was additionally collected.

Inclusion and Exclusion Criteria

Case Group: Pediatric patients with COVID-19 toes without psoriasis (and without any other chronic or acute comorbidities such as, interstitial bilateral pneumonia, dyspnea, or sensorial loss (ageusia or anosmia).

Control Group: PsO patients with a disease duration >2 years without acute or chronic comorbidities⁶, such as COVID-19⁷⁻⁹, that were under the prescribed anti-psoriatic systemic treatment¹⁰.

Patients Excluded: (a) Patients that underwent a particular diet or fasting during the study or 1-month before¹¹⁻¹³, (b) Patients that interrupted, modified, or discontinued the prescribed dermatological treatment, (c) Patients that did not perform a serological SARS-CoV-2 test after COVID-19 toes.

Dermatological Assessment

Patients were assessed by two independent, board-certified dermatologists with both in person and teledermatological visits (FaceTime®). Each patient's parent underwent the DFI questionnaire that comprehend 10 questions scored 0-3 points each (0=not at all, 1=a little, 2=a lot, 2 very much) with a maximum score of 30 points¹⁴.

PsO patients were also assessed with Psoriasis Area Severity Index (PASI) and itch-Visual Analogue Scale to evaluate disease extension and pruritus, two well-known determinants of stigmatization^{15,16}.

Statistical Analysis

The type of distribution for all variables was analyzed by Kolmogorov-Smirnov test. Statistical comparisons were carried out by independent Student *t*-test while the Pearson correlation coefficient was analyzed to investigate any statistical association. The influence of independent predictors on indexes (PASI, itch_VAS and DFI) was evaluated by multiple regression analysis (enter approach). Results are reported as mean ± standard deviation (SD), median or percentages (%). Analyses were carried out by using the MedCalc Statistical

Software version v19.0.5 (MedCalc Software bvba, Ostend, Belgium) and *p*-value < 0.05 was considered significant.

Results

In this study, a total number of 46 pediatric patients (23 with psoriasis and 23 with COVID-19 toes) were enrolled. In Table I, demographics and clinical data are reported for both subgroups. Interestingly, DFI index did not significantly differ between both subgroups (*p*=0.48).

In psoriatic patients no correlation was observed between itch_VAS and DFI (*p*=0.16), itch_VAS and PASI (*p*=0.29) or DFI and PASI (*p*=0.59). DFI index was not influenced by the age or sex, the involvement of special location, the type of treatment, or the number of siblings (*p*=0.71). Similarly, the same variables did not influence the levels of itch_VAS (*p*=0.87) and PASI (*p*=0.44) index in this psoriatic subgroup. When these patients were further subdivided based on the type of therapy (biological or non-biological therapy), a lower PASI index was observed for those treated with biological therapy (*p*=0.04), while no difference was reported for DFI and itch_VAS (Table II).

In patients affected by chilblain-like, no correlation was observed between the DFI index, and the number of fingers involved (*p*=0.96). DFI was not influenced by the age or sex, the number of siblings as well as the number of other familiars affected by COVID-19 (*p*=0.29).

Discussion

COVID-19 pandemic represents a serious challenge for healthcare systems worldwide¹⁷⁻¹⁹ that must restructure their hospitals and ambulatories based on the available evidence and health priorities²⁰. In this scenario, dermatological patients were often deprioritized, unless they underwent systemic immunosuppressants or had a diagnosed skin cancer^{21,22}, and dermatologists were forced to use teledermatology for the other patients²³. Thus, asymptomatic pediatric patients with COVID-19 toes were often evaluated with telemedicine together with their parents.

COVID-19 toes, a transitory dermatosis widely publicized by media, exerted a similar impact/perturbation on family dynamics than PsO, a chronic inflammatory dermatosis. The spread

Table I. Demographic and clinical data reported for patients affected by psoriasis (n = 23) and chilblain like (n = 23).

Variable	Psoriasis (N = 23)	Chilblain-Like (N=23)	p-value
Age, mean ± SD (median), years	11.95 ± 3.02 (12.00)	11.56 ± 2.62 (12.00)	0.64
DFI, mean ± SD (median)	18.35 ± 4.89 (18.00)	19.22 ± 3.20 (19.00)	0.48
Gender, N (%)	Male: 13 (56.52%) Female: 10 (43.48%) Non-binary gender: 0 (0.0%)	Male: 13 (56.52%) Female: 10 (43.48%) Non-binary gender: 0 (0.0%)	1.00
Itch VAS, mean ± SD (median), mm	6.61 ± 1.70 (7.00)	/	/
PASI, mean ± SD (median)	4.78 ± 1.95 (4.00)	/	/
Involvement of special locations, N, (%)	Genitals: 3 (13.04%) Hands: 4 (17.39%) Head and hands: 7 (30.44%)	/	/
Psoriatic Therapy, N, (%)	Adalimumab: 9 (39.13%) Etanercept: 2 (8.70%) Ixekizumab: 1 (4.35%) NB-UVB: 6 (26.09%) Secukinumab: 5 (21.73%)	/	/
Siblings, N, (%)	0 siblings: 5 (21.74%) 1 sibling: 14 (60.87%) 2 siblings: 3 (13.04%) 3 siblings: 1 (4.35%)	0 siblings: 8 (34.78%) 1 sibling: 10 (43.48%) 2 siblings: 4 (17.39%) 3 siblings: 1 (4.35%)	0.71
Fingers of feet involved, N, (%)	/	0 finger: 8 (34.78%) 1 finger: 1 (4.35%) 2 fingers: 8 (34.78%) 3 fingers: 4 (17.39%) 4 fingers: 2 (8.70%)	/
Fingers of heads involved, N, (%)	/	0 finger: 8 (34.78%) 1 finger: 1 (4.35%) 2 fingers: 5 (21.74%) 3 fingers: 6 (26.09%) 4 fingers: 3 (13.04%)	/
Other COVID-19 affected familiars, N, (%)	/	No: 4 (17.39%) 1 familiar: 9 (39.13%) 2 familiars: 9 (39.13%) 3 familiars: 1 (4.35%)	/

Abbreviations - DFI: Dermatitis Family Index, PASI: Psoriasis Area and Severity Index, SD: Standard deviation, VAS: Visual Analogue Scale.

of the COVID-19 pandemic has led to an increase of COVID toes reports, since their prognostic value were not fully clarified²⁴. Despite the pathogenetic and therapeutic uncertainties, COVID-19 toes elicit stigmatization on the pa-

tient and on his/her family members that had to quarantine for 15 days.

Their clinical appearance may remind to perniois or vascular ulcers, two conditions may be differentiated to COVID-19 toes only with biopsy,

Table II. Itch VAS, PASI and DFI indexes reported for psoriatic patients under biological and non-biological therapy.

Variable	Non-biological therapy (n = 6)	Biological therapy (n = 17)	p-value
Itch VAS, mean ± SD (median), mm	6.67 ± 1.75 (7.50)	6.59 ± 1.73 (7.00)	0.92
PASI, mean ± SD (median)	6.17 ± 2.48 (7.50)	4.29 ± 1.53 (4.00)	0.04
DFI, mean ± SD (median)	17.83 ± 5.38 (18.00)	18.53 ± 4.86 (17.00)	0.77

Abbreviations - DFI: Dermatitis Family Index, PASI: Psoriasis Area and Severity Index, SD: Standard deviation, VAS: Visual Analogue Scale.

an invasive approach difficult to perform during pandemic. Thus, clinical evaluation together with a recent medical history of cough and fever remain suggestive to a COVID-19 toes diagnosis. Clinically, hand lesions appear erythematous, erythematous-violet, or erythematous-infiltrative lesions, lupus pernio-like (Figure 1 A-B). Lesions on the feet appear more erythematous violet, infiltrated, sometimes vesicobullous, seldom hemorrhagic with a crusty evolution on the toes. Lesions usually affect the entire toe with distal-proximal progression, occasionally skipping the consecutive one; hemorrhagic lesions involving peri-matrix areas may cause dystrophic nails or, rarely, even onychomadesis. Hair may be transiently lost in the affected areas. The metatarsophalangeal area is usually not involved or demarcated by few round purpuric elements; conversely, in calcaneus lesions appear smaller, red-to-violet with multi-focal roundish elements, plantar lesions often appear coarse, erythematous-violet and infiltrated (Figure 1 C-D). These clinical manifestations have been associated with COVID-19 from a temporal point of view; however, clear evidence regarding its pathogenetic mechanism is still lacking²⁵.

Nevertheless, it has been reported that these lesions tend to mainly effect children, adolescents, and young adults and are increasingly being reported as the most specific COVID-19 cutaneous manifestation. Overall, it is well described in the literature that pediatric dermatological diseases, such as psoriasis, can negatively impact both patients' and families' quality of life.

Parents and caregivers' commitment is crucial in both short and long-term dermatological treatment of pediatric patients²⁶⁻²⁹, so DFI may be routinely used in pediatric dermatology to monitor family environment and indirectly also patients' compliance. Furthermore, perturbations of family dynamics during childhood and adolescence have been associated with long-term psychiatric sequelae, such as anxiety and depression²⁹. Remarkably, both psoriasis and COVID-19 have an imponent psychiatric burden, that spaces from depression to Cabin Fever syndrome and deeply influence both daily functionality and treatments administration³⁰⁻³³.

Conclusions

In conclusion, the authors of this study suggest to carefully monitor and quantify with DFI or other scores also the family environment in both

transitory and chronic dermatoses. Limitations of this study include small number of subjects to reach a certain statement, further studies are needed in literature with larger number of groups.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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None.

Consent to Participate

Consent to Participate.

Ethics Approval

The studies on COVID-19 disease are approved by all Local Ethical Committees due to the emergency. No additional permission was needed.

Availability of Data

Data is available upon request.

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None.

Authors' Contribution

G.D., R.F., K.K., A.P., N.L.B., P.M., G.F., E.B., F.M., C.L., P.S., L.C.G., M.M., T.D., A.W., F.G., C.M., and M.D. F. conceived and designed the analysis. All the authors contributed on analysis and interpretation of data for the work. All authors revised the work critically for intellectual content. Integrity of the work was appropriately investigated and resolved by all authors. All authors contributed and approved equally to the final version of the manuscript.

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