



MICRO LABS LIMITED

# Derma Today

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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you “**Derma Today**” which contains latest and interesting news in the field of Dermatology.

This issue contains:

1. Analysis of Chilbain like lesions in COVID 19 infection.
2. Study of Effect of Biological Agents on Antinuclear Antibody Status in Patients with Psoriasis
3. An uncommon clinical presentation of prurigo nodularis-like lesions in a Patient with Lepromatous Leprosy.

Should you require any article or, medical information, please feel free to contact us [medicalservices@microlabs.in](mailto:medicalservices@microlabs.in)

Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited.

## Analysis of Chilblain like lesions in COVID 19 infection

### Introduction

Cutaneous manifestations, including chilblain-like lesions, are with severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) infection during the coronavirus 2019 (COVID-19) pandemic, whose pathophysiology is not clear.

This study aimed to perform a methodical, prospective evaluation of patients with chilblain-like lesions to characterize the condition during the pandemic times.

### Methods

Forty patients suspected of having COVID-19 were suspected to have skin-manifestations linked to COVID-19. patients were evaluated for chilblain. Patients showing signs of chilblain disease underwent systematic blood cell counts, liver and kidney function, prothrombin time, partial thromboplastin, time, erythrocyte sedimentation rate, C-reactive protein levels-dimer values, antinuclear antibodies, antiphospholipid antibodies, haemolytic complement (C3, C4, CH50), Cryoglo- bulinemia, parvovirus serology, and interferon-alpha (IFN- $\alpha$ ) stimulation and detection.

Proteinuria, leucocyturia and haematuria evaluated through urine tests. SARS-CoV-2 was tested by real-time polymerase chain reaction (rt-PCR). Skin biopsy was performed. The European Centre for Disease Prevention and Control and prevention for COVID-19 case definition and the World Health Organization scale for severity were used.

### Results

Of the 42 patients clinical presentation was highly reproducible with chilblain-like lesions mostly on the toes. Clinical presentation displayed a similar clinical pattern beginning with pruritus, and pain of toes, occasionally heels and fingers, followed by pink-to-red papules or plaques that progressed to violaceous purpuric lesions with frequent bullous and necrotic evolution.



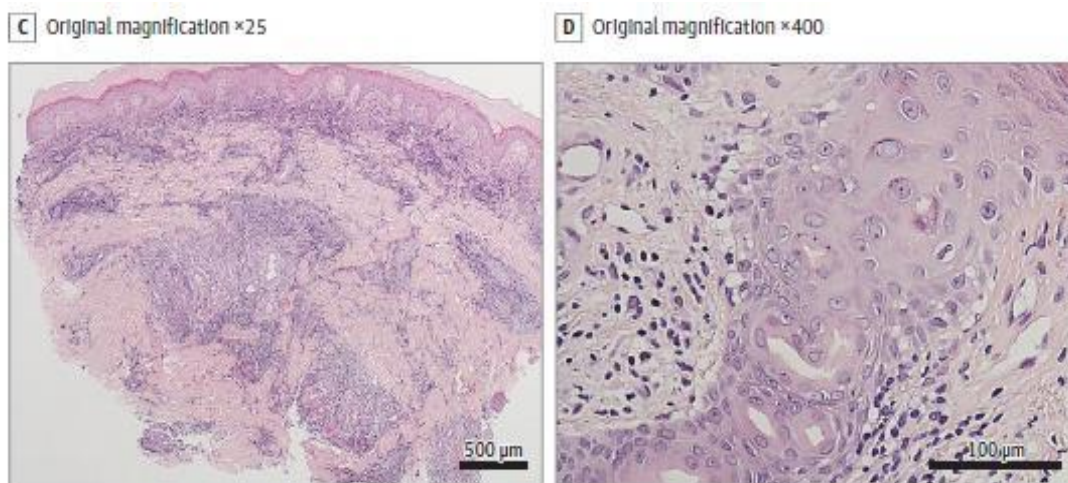
**Figure 1: A-Red-to-violaceous purpuric lesions on the toes. Note the bullous and necrotic evolution. B- Red-to-violaceous papules with marked bullous evolution**

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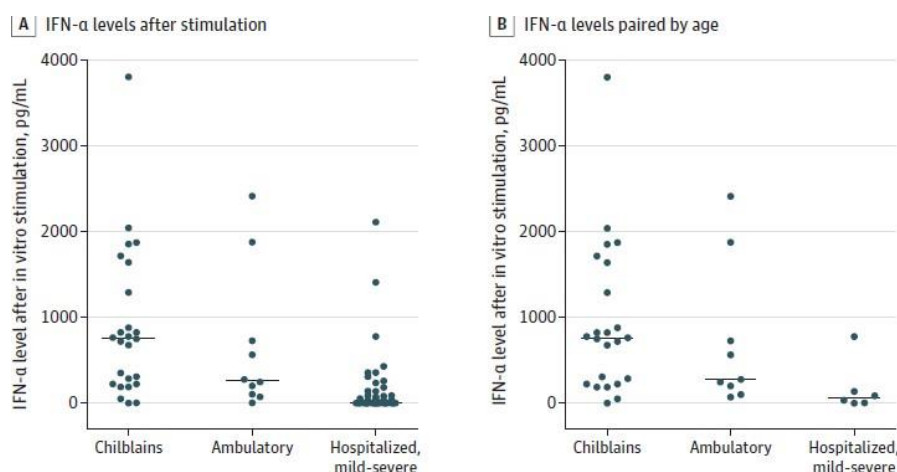
Acrocyanosis (cyanotic extremities) or cold toes were reported in 18 (47%) cases. Criteria compatible with COVID-19 cases were observed in 10 (27%) within 6 weeks before the eruption. The real-time PCR (rt-PCR) testing results were negative in all cases. 11(25%) patients were tested positive in SARS-CoV-2 serology tests. The major histologic findings presented with features of lymphocytic inflammation and vascular damage with thickening of venule walls and pericyte hyperplasia.

**Figure1: C-Dense superficial and deep lymphocytic inflammation with perivascular and peri-eccrine arrangement (hematoxylin-eosin stain). D-Interface dermatitis extending to the intra-epidermis portion of acrosyringium (hematoxylin-eosin stain).**

A



significant increase of IFN- $\alpha$  production after in vitro stimulation was observed in the chilblain population compared with patients with PCR-positive acute COVID-19 with a range of severity (mild-severe) (Figure 2A). The results did not change when patients were paired for age (Figure 2B).



**Figure2: Comparison of IFN-  $\alpha$  Response in Chilblain Population With Ambulatory and Hospitalized Mild or Severe Cases of Coronavirus Disease 2019 (COVID-19)**

## Discussion

Chilblains lesions occurrence in 40 patients, corresponded with the spread of SARS-CoV-2. Though there was no strong evidence linking chilblains with COVID-19 infection, it would be important to note that, decreased test sensitivity has been noticed in patients with asymptomatic COVID-19 infection, and an alternative immunologic or infectious cause for these transient chilblain-like lesions was not identified in this study group.

Majority of the patients were adolescents and young adults without additional medical problems and chilblain-like changes resolved in all the cases.

The chief finding of the study is that the biologic, histologic and clinical findings were indicative of virus-induced type I interferonopathy. Severe chilblains associated with bullous lesions and necrosis can occur in type I interferonopathies. IFN- $\alpha$  response was greater in chilblains compared to those with moderate or severe COVID-19. The exaggerated type I interferon response might be suggestive of the relatively low rate of seropositivity in patients with chilblains as those patients could clear SARSCoV-2 infection before humoral immunity sets in.

## Conclusion

Chilblain-like lesions observed during the COVID-19 pandemic, shows the characteristics of a viral-induced type I interferonopathy. Type of immune response becomes an important factor which describes the diversity of clinical manifestations observed in COVID-19 infection.

### Reference:

Hubiche T, Cardot-Leccia N Et al. Clinical, Laboratory, and Interferon-Alpha Response Characteristics of Patients With Chilblain-like Lesions During the COVID-19 Pandemic. JAMA Dermatol. 2020 Nov 25.

## Study of Effect of Biological Agents on Antinuclear Antibody Status in Patients with Psoriasis?

### Introduction

Biological agents have been the mainstay of treatment of psoriasis for many years. But, there are possibilities of developing autoimmunity upon using these agents. Certain factors such as the type of the disease and immunosuppression brought about these agents, affects the changes in Antinuclear antibody (ANA) levels. Hence, this study aimed to determine the effect of antitumor necrosis factor

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agents and ustekinumab on ANA status, along with other factors leading to change in ANA status like history of phototherapy and combination therapy with methotrexate.

## Methods

The laboratory findings of thirty-one patients who were on treatment with biological agents including infliximab, etanercept, adalimumab and ustekinumab from Dec 2016-2018 at the department of Dermatology were reviewed. The patients were ANA-negative before the initiation of the therapy. Therapy with biological agents was initiated if the patients exhibited resistance to the existing treatments due to inefficacy, conventional treatments were not appropriate due to safety issues, and the disease lasted at least 6 months with Psoriasis Area and Severity Index score (PASI) >12. The ANA status was evaluated periodically every 2-3 months.

The biological agents were administered in accordance with the standard recommended dosage protocols for psoriasis. Infliximab was administered intravenously at 5 mg/kg at baseline, after 2 and 6 weeks, followed by every 8 weeks. The dose of UST for an adult patient with psoriasis weighing up to 100 kg was 45 mg (one injection) at the initial week, one injection at week 4, and then an injection once every 12 weeks from then on. For patients weighing more than 100 kg, the dose was 90 mg (two injections) and was given at the same time intervals as the lower dose schedule (i.e., week 0, week 4, and then every 12 weeks from then on). Etanercept dose for induction was 50 mg once a week. The initial loading dose of ADA was 80 mg, followed by 40 mg every other week starting one week after the initial dose.

Indirect immune-fluorescence assay (IIFA) was used for screening of ANA status.

Patients were also studied for concomitant use of Methotrexate along with biological agents and any history of phototherapy (narrow-band UVB and psoralen-UVA). The dose of methotrexate was 7.5mg weekly.

## Results

Twelve patients (38.7%) showed ANA positivity during the treatment. The nuclear homogeneous, nuclear fine speckled, and nuclear large/coarse speckled were the observed as the most common patterns of ANA.

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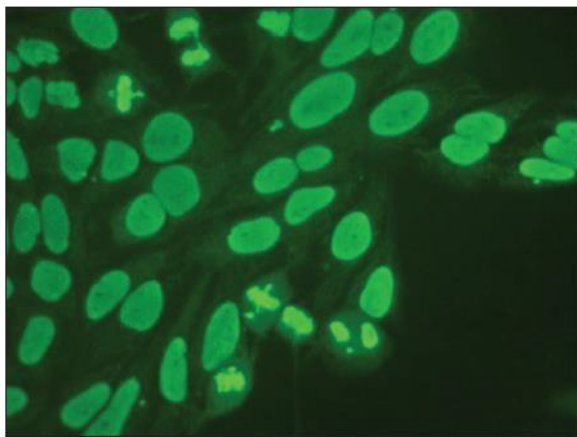


Figure 1: The nuclear homogeneous pattern in ANA positivity

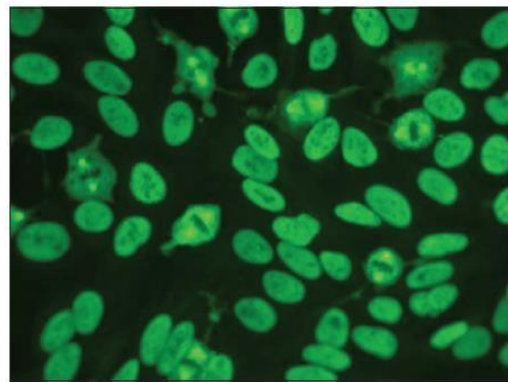


Figure 2: The nuclear large/coarse speckled pattern in ANA positivity

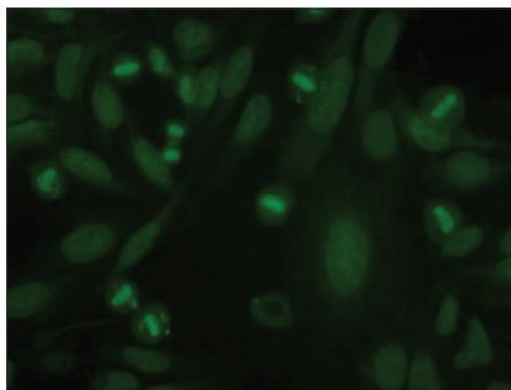


Figure 3: The nuclear fine speckled pattern in ANA positivity

Nine patients administered with infliximab, two patients administered etanercept, and one patient receiving adalimumab exhibited ANA positivity (Table-2). A patient receiving infliximab also developed anti-dsDNA positivity. None of the patients developed drug-induced lupus erythematosus or any autoimmune diseases. Concomitant methotrexate use and phototherapy history had no effect on ANA status statistically ( $P = 0.240$  and  $0.717$ , respectively).

## Discussion

Ustekinumab and anti-TNF agents including IFX, ETC, and ADA are the most commonly used agents in psoriasis. These agents have been implicated to produce auto-antibodies against DNA and other nuclear antigens, which might lead to the development of lupus erythematosus which is usually rare. ANA is used as a screening test for the diagnosis of autoimmune diseases. About 25% of the population show ANA positivity, but the prevalence of significantly greater levels was 2.5%. None of patients

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developed clinical signs and laboratory investigation including ANA, anti-dsDNA for an autoimmune disease or drug-induced lupus with a follow-up period of 2 years following ANA positivity. Though TNF- $\alpha$  blockers, are drugs that have recently been reported to induce lupus, with the findings of this study it can be considered that biological agents may be effective in patients with psoriasis from the perspective of autoimmunity.

## Conclusion

The occurrence of ANA positivity during infliximab therapy compared to all biological agents was more common. ANA positivity during biologic agents is not associated with any signs and symptoms of autoimmune diseases in patients with psoriasis; thus, it can be suggested that biological agents do not carry the risk of auto-immunity.

*Kutlu Ö, Çetinkaya P Et al. The effect of biological agents on antinuclear antibody status in patients with psoriasis: A single-center study. Indian Dermatol Online J 2020;11:904-9.*

## An uncommon clinical presentation of prurigo nodularis-like lesions in a Patient with Lepromatous Leprosy

### Case study

Lepromatous leprosy(LL), a chronic infectious disease mainly affects the peripheral nerves and the skin. Clinical manifestations range from hypopigmentation to erythematous plaques, and present with leonine facies.

Following is the case of an Asian male patient who presented with a prolonged-period of clinically identified prurigo nodularis and who had the two dermatopathological subtypes of LL based on his skin manifestations.

#### Case report

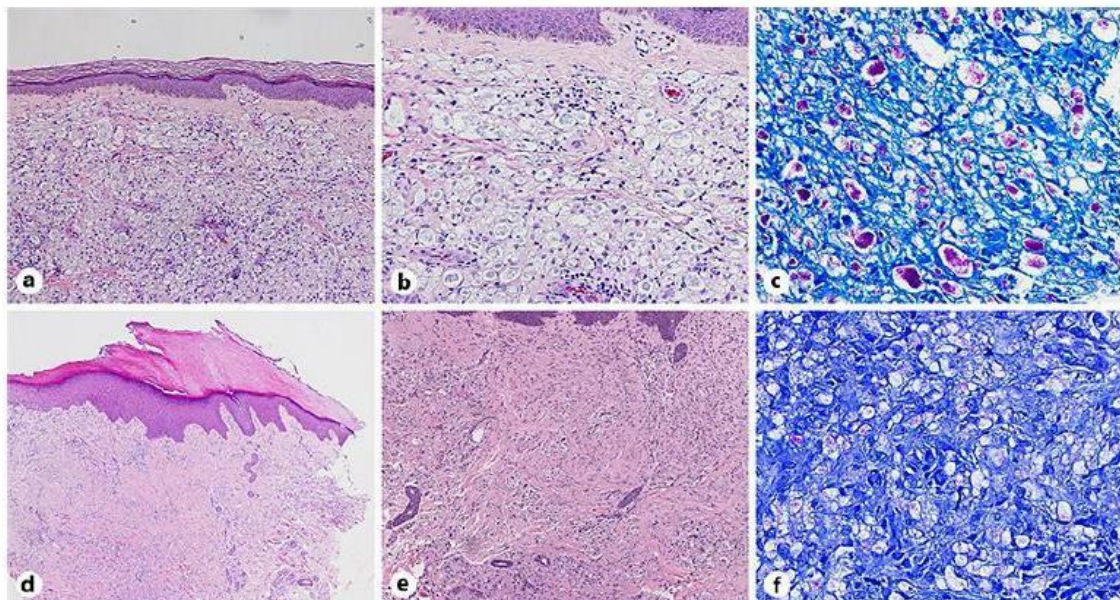
A 68-year old man presented with a number of itchy papules on the legs, torso and upper extremities since 2 years. Priorly he was treated with anti-histamines, topical corticosteroids and a short course of systemic steroids, which showed low prognosis.

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The patient had a history of various co-morbidities such as hypertension, coronary artery disease, hypertrophic cardiomyopathy and gouty arthritis. His present medications include aspirin, clopidogrel, carvedilol, nifedipine, simvastatin, omeprazole, colchicine, and warfarin.

Dermal examination showed multiple, hyperpigmented papules with central erosions and crusts spread on the abdomen and extremities. Neurological examination showed no loss of sensation.

Two skin biopsy sample from the right arm were performed. The first sample obtained from a lesion with an erythematous papule, showed a normal dermis and the dermis revealed diffuse foamy infiltrates with globi formations and presence of a Grenz zone. Fite's staining showed a positive result for the presence of a bacilli. The second sample taken from a hyperkeratotic papule showed irregular acanthosis of the epidermis. Diffuse fusiform and foamy histiocytic infiltrate with several globi formations was noticed in the dermis. Grenz zone was not detected in this section and Fite's staining showed positive for the presence of bacteria.



Skin biopsy specimens from the left upper arm. **a–c** From erythematous papules. **a, b** The dermis shows a diffuse foamy histiocytic infiltrate with globi formation and the appearance of a Grenz zone (H&E, **a** 20×, **b** 40×). **c** Fite's stain was strongly positive, showing numerous bacilli (Fite's stain, 60×). **d–f** From hyperkeratotic papule. **d** The keratin exhibited compact orthokeratosis with mild irregular acanthosis of the epidermis (H&E, 4×). **e** Diffuse fusiform and foamy histiocytic infiltrate, several globi formations in the dermis, and the histiocytes arranged in a whorled pattern at the dermis (H&E, 20×). **f** Fite's stain was strongly positive (Fite's stain, 60×).

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Patient was started with a modified WHO-recommended multidrug therapy regimen (rifampicin, dapsone, and clofazimine) for 24 months. After 6 months of treatment, improvement was seen in his skin lesions and itching symptoms, in addition to the absence of leprosy reactions.

## Discussion

Patient was initially treated for prurigo nodularis. However, the diagnosis was difficult as absence of loss of sensation and local nerve enlargement were unusual characteristics of leprosy. This necessitated histopathological studies. The two samples showed prurigo nodularis-like lesions which exhibited a typical LL and a rare variant type of LL, HL. The two different histological patterns clinically resembling prurigo nodularis, which makes it enigmatic to diagnose leprosy; this finding can also lead to the prevalence of the disease if appropriate differential diagnosis is not performed.

Atypical presentations must lead to suspicion among the physicians about HL. The histopathology of HL reveals spindle-shaped histiocytes predominantly, forming interlocking bands, whorls, or storiform patterns and numerous acid-fast bacilli. The epidermis overlying the lesion is generally atrophied.

To date, there is no standard guideline for HL, but the existing treatment for multi-bacillary leprosy can be used for a patient with HL.

## Conclusion

HL is rarely associated with LL. This is a novel case of HL clinically mimicking prurigo nodularis. Knowledge about the atypical manifestations and precise differential diagnosis, might provide suggestions and recommendations to clinicians and researchers which would clarify this form of leprosy mimicking prurigo nodularis, when the patients presents with lepromatous features such chronic recalcitrant itching papules and nodules, thus leading diagnosis of leprosy.

**Source:** Nawalerspanya S, Sangmala S, Aiempanakit K. A Case Report of Prurigo Nodularis-Like Lesions in a Patient with Lepromatous Leprosy. Case Reports in Dermatology. 2020;;236-240.



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