

BRIEF ARTICLES

A Case Report of Chilblain Lupus Erythematosus in a Young Male with Literature Review

Azib Shahid MD,¹ Katherine Glaser MD,² Anthony Fernandez MD²

¹Rosalind Franklin University, North Chicago, Illinois

²Cleveland Clinic, Cleveland, Ohio

ABSTRACT

Chilblain lupus erythematosus (CHLE), also known as Hutchinson lupus, is rare form of chronic cutaneous lupus erythematosus. The diagnosis is made in patients with clinical findings of chilblains in conjunction with the clinical or laboratory features of cutaneous or systemic lupus erythematosus (SLE). Similar to idiopathic chilblains (or perniosis), CHLE presents with tender, reddish-blue papules, nodules, or plaques on the toes, fingers, nose, or ears which are precipitated by cold exposure. There is a variation in lab findings that become positive in these patients ranging from a positive Antinuclear antibody (ANA), Rheumatoid factor (RF), SSA/Ro autoantibodies. Anemia, hypocomplementemia, other autoantibodies and elevated ESR have also been described in numerous patients. Sporadic disease commonly affects middle-aged women whilst familial disease manifests in childhood. We report herein, a case of CHLE in a young male with no family history of lupus and a negative ANA on initial evaluation. There is little in the published literature on CHLE. This case report serves to revisit the diagnosis of CHLE and review the existing literature. Clinicians should understand the importance of early diagnosis and prompt treatment initiation in order to reduce associated morbidity and possible disfigurement.

INTRODUCTION

Chilblain lupus erythematosus (CHLE) is a rare, chronic, skin disorder considered a form of chronic cutaneous lupus erythematosus. Patients with CHLE have skin lesions that are clinically consistent with chilblains and clinical or laboratory features of cutaneous or systemic lupus erythematosus. Ages at onset of chilblain lupus erythematosus varies from 26 to 73 years, with a female-to-male ratio of 3:2. The diagnosis of CHLE was first described in 1888 by Jonathan Hutchinson.¹ According to a comprehensive literature

review published in 2008, only about 70 cases have been reported since.²

Skin findings of CHLE consist of erythematous to violaceous papules, plaques, or nodules. Initially they may be described as pruritic but eventually become painful.²⁻⁶ The lesions appear during cold or damp periods and do not remit during warmer seasons.³ Cutaneous lesions occur predominately on acral surfaces and sites exposed to cold such as the nose, ears, elbows, and knees. Isolated involvement of the 5th digits has been described.^{2,4,7} Fissural hyperkeratosis and central ulceration may

occur in lesions. Nailfold capillaroscopy typically reveals changes in proximal nailfold capillary morphology, with enlarged and tortuous capillary loops being a common finding.^{4,5} Chilblain lesions may also be accompanied by discoid or subacute cutaneous lupus erythematosus lesions.

The etiology of this disorder may be familial or sporadic. A missense mutation in the TREX1 gene which encodes for 3'-5' repair exonuclease enzyme has been described in familial cases. TREX1 deficiency was shown to cause intracellular accumulation of single-stranded DNA which may originate from DNA repair processes or the life cycle of endogenous retro-elements. It is thought that recognition of these inappropriately accumulated nucleic acids by the innate immune system leads to a type I IFN response that subsequently induces autoimmunity. This variant is characterized by onset of lesions early in infancy or adolescence.²

The pathogenesis of the sporadic form remains unknown. Hypotheses have speculated a disorder of peripheral circulation resulting in either inappropriate vasoconstriction or microvascular injury associated with capillary bed occlusion, hyperviscosity, and stasis. Platelet adhesiveness and aggregation are increased by cold and may contribute by promoting sluggish blood flow. Common associations like hypergammaglobulinemia and rheumatoid factor may favor hyperviscosity. Some reports also note an association with antiphospholipid antibody syndrome, suggesting hypercoagulability may also play a role. In support of this hypothesis, angi-MRI studies in at least one patient revealed reduced phalangeal perfusion.² A peripheral circulation disorder could explain why some cohorts have significantly higher incidence of Raynaud's phenomenon.

To help delineate CHLE from other cold-induced dermatoses, the Mayo Clinic has proposed a useful diagnostic criteria.⁸ Using the Mayo Clinic Diagnostic Criteria the diagnosis of CHLE can be made if two major and at least one minor criteria are met. These include:

Major criteria:

- 1) Acral skin lesions associated with cold temperature
- 2) Evidence of lupus erythematosus in skin lesions on histopathology or direct immunofluorescence

Minor criteria:

- 1) Coexistence of systemic lupus erythematosus or other skin lesions of discoid lupus erythematosus
- 2) Response to anti-lupus erythematosus therapy
- 3) Negative results of cryoglobulin and cold agglutinin studies.

Treatments for CHLE include antimalarial agents, prednisone, pentoxifylline, nifedipine, and dapsone are reported to be beneficial. Behavioral modifications should also be instituted including sun protection, avoidance of cold, and smoking cessation. Acupuncture, yoga, and meditation have also shown to be beneficial in some cases. Acupuncture however should not be used in children.^{3,8}

CASE PRESENTATION

A 27 year old male presented to the dermatology department with a 10 year history of a painful purpuric rash and few ulcerations on the bilateral hands, elbows, face, ears, and extensor surfaces of knees. Lesions worsened with cold temperatures and stress. Associated symptoms included fatigue, subjective weight loss, intermittent arthralgias, subjective fevers, and Raynaud's phenomenon. Otherwise review of systems

January 2020 Volume 4 Issue 1

was negative. He was previously diagnosed with discoid lupus erythematosus and treated as such with Hydroxychloroquine and topical steroids with some improvements. Hydroxychloroquine was subsequently discontinued due to intolerable gastrointestinal symptoms thus his presentation for additional treatment options.

The patient's history is significant for known idiopathic thrombocytopenic purpura diagnosed at age 12. After treatment with intravenous immunoglobulin, systemic steroids, and later Rituximab he has since remained in remission. Ongoing mild leukopenia and thrombocytopenia are being monitored by his Hematologist. Family history was remarkable for scleroderma in his mother. No other contributory history was identified.

On examination he had multiple red to violaceous papules and plaques with few central erosions and overlying hemorrhagic crust on the nose, medial cheeks, antihelices, dorsal hands, dorsal fingers over joint spaces, anterior knees, and palmar surfaces of the fingers and toes (Figures 1-4). Few small smooth alopecic patches on the parietal scalp were noted. Multiple atrophic hypopigmented macules were seen scattered over the upper back. Mucosal surfaces were not affected.

Prior to presentation his laboratory work-up showed a minimally elevated double stranded DNA autoantibody level but was otherwise unremarkable. Work-up included an antinuclear antibody (ANA), extractable nuclear antigen autoantibody panel (ENA), cryoglobulin levels, complement three and four levels, serum protein electrophoresis, urinalysis, hepatitis panel, hypercoagulability panel, and a specific myositis panel to screen for dermatomyositis. Repeat laboratory work-up during his visit now showed positive ANA

and positive anti-chromatin autoantibody with chronic mild leukopenia and thrombocytopenia. The remaining ENA panel was negative and notably cold agglutinins were within normal limits.

Outside skin biopsy reports could not be obtained so a repeat punch biopsy was performed from the patient's right knee. The specimen revealed focal areas of parakeratosis within the stratum corneum and focal vacuolar interface changes with scattered necrotic keratinocytes in the epidermis. Within the dermis a superficial and deep perivascular and peri-eccrine lymphocytic infiltrate was identified. Mucin was also present throughout the interstitial space (Figures 5,6).

The above histopathologic features in combination with the clinical presentation were deemed compatible with the diagnosis of chilblains lupus. Our patient was advised on proper preventative measures. Treatment was initiated with topical clobetasol 0.05% ointment, low dose Amlodipine 2.5mg daily, Pentoxifylline 400mg three times daily, and Chloroquine 250mg once daily given his prior side effects with hydroxychloroquine. He plans to follow up with our dermatology department for further monitoring.

Figure 1. Hands Before



Figure 2. Hands After



Figure 3. Left Foot Before



Figure 4. Left Foot After



Figure 5. Biopsy 4x

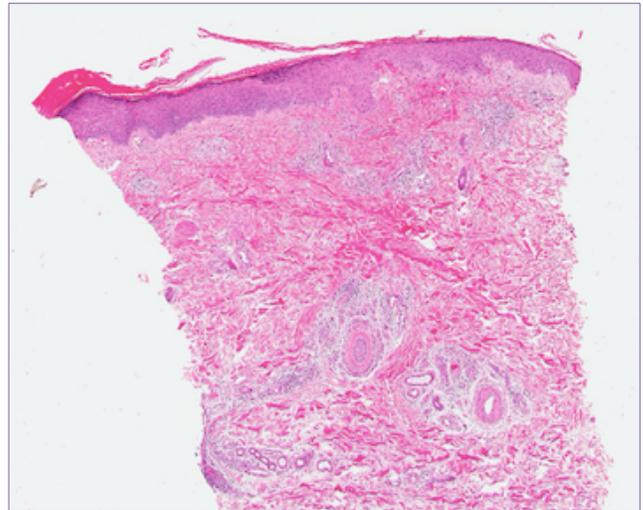
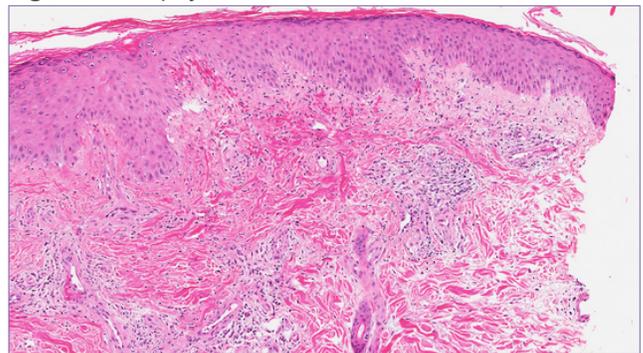


Figure 6. Biopsy 40x



DISCUSSION

Chilblains (also known as Pernio or perniosis) is a condition characterized by the development of cold-induced erythrocyanotic skin lesions. The word "chilblains" may be derived from the Old English words "chill" and "blegen" (sore).² Literature on CHLE describes association of this disorder with several other conditions that are discussed below. So we recommend a thorough evaluation of all presenting signs and symptoms, a detailed family history, comprehensive lab evaluation and early diagnosis which are the cornerstones in the management of this disorder.

Chilblain lupus is relatively uncommon. In a cohort of 308 patients with cutaneous lupus, chilblain lupus was found in only 9.3% of females and 1% of males.⁶ Women seem to be predominantly affected, but this may reflect higher general tendency for women to be affected by lupus erythematosus.

ANA is typically positive and tends to be a speckled-pattern.⁷ At least one study suggested presence of SSA/Ro autoantibodies were significantly common in chilblain lupus patients.⁵ In other studies, however, only a minority of patients have SSA/Ro autoantibodies.^{3,4,8,9} Hypergammaglobulinemia is observed >66% patients and Rheumatoid factor is present in ~50%.^{2,4,7} Anemia, hypocomplementemia, other autoantibodies and elevated ESR have also been described in numerous patients.^{3,7} Pancytopenia in association with chilblain lupus has been rarely described.¹⁰

CHLE is associated with presence or progression to SLE in about 18-20% of patients, and chilblain lupus lesions may occur prior, concurrently, or subsequent to SLE diagnosis.^{5,2} In general, SLE patients with chilblain lupus lesions tend to have relatively mild systemic involvement and low prevalence of renal involvement.¹ Approximately 25 percent of patients who present with chilblains meet classification criteria for SLE, and additional patients (5 to 6 percent in one study) may fulfill SLE criteria subsequently. Observations from a series of 33 patients with chilblains that included patients with chilblain lupus erythematosus suggest that persistence of skin lesions beyond cold seasons may be more frequent in patients with chilblain lupus erythematosus.³ This was also observed in our patient.

The most frequently reported and most studied relationship between chilblains and

another disease is the relationship between chilblains and lupus erythematosus. Multiple reports describe the development of skin lesions that are clinically consistent with chilblains in patients with clinical or laboratory evidence of cutaneous lupus erythematosus or systemic lupus erythematosus.²⁻⁷ Less commonly reported association includes pregnancy induced chilblain lupus.¹¹ An association with anorexia, intestinal lymphoma and chronic myelomonocytic leukemia has also been reported but not conclusively proven.¹²⁻¹⁴ According to the literature, it is not completely apparent whether all reported patients had normal values for cryoglobulins, cold agglutinins and cryofibrinogens in chilblains lupus.¹⁵ All these values were found to be negative in our patient.

Histology is typically characterized by a superficial and deep perivascular lymphocytic infiltrate. Vacuolar interface changes are also seen in many lesions. DIF may reveal deposition of immunoglobulins, complement, or a lupus band at the dermal-epidermal junction.¹² The main differential diagnosis is with idiopathic chilblains or perniosis. Studies suggest histologic findings that may favor CHLE include spongiosis (not observed in LE), vacuolation of the basal cells (more frequent in LE), perieccrine inflammation (uncommon in LE), and presence of dermal edema (much more frequent in idiopathic chilblains).^{9,16} Numerous studies have particularly stressed absence of perieccrine inflammation in CHLE compared to idiopathic chilblains.^{9,16} Necrotic keratinocytes and vacuolar change can be seen in idiopathic chilblains.^{9,16} These distinguishing features have not been found in all studies and distinction based only on histopathology is not always possible. Diagnosis should be correlated with clinical and serologic data. A clinical review by Su WP et al. that reviewed 5 patients and developed the diagnostic criteria discussed

earlier concluded that chilblain lupus erythematosus lesions are slower to respond to treatment compared to discoid lupus erythematosus. Treatment with antimalarial agents, prednisone, pentoxifylline, or dapson was found to be beneficial in their patients.⁸ Other treatment options include protection from cold by physical measures and the use of oral or topical antibiotics if the lesions get infected. We used calcium channel blockers and topical steroids in our patient which proved to be effective in clearing out the skin lesions. Efficacy of nifedipine (a calcium channel blocker) for treating chilblains is evident in literature.¹⁷

CONCLUSION

Chilblain lupus erythematosus is a rare diagnosis that can be difficult to make. It is important to rule out other cold induced syndromes prior to initiating therapy. Chilblain lupus is persistent, thus once lesions have developed they may take 4 to 6 months to resolve. All patients newly diagnosed with CHLE should be counseled on the specific disease course, including any potential risk for scarring and disfigurement and should be reassured that their disease progression is relatively benign. In a patient diagnosed with chilblain lupus, the treatment goal is to prevent development of new lesions and expedite the healing of current lesions in order to avoid discomfort and scarring. All patients should be encouraged to stop smoking and begin a smoking cessation program. The risk of developing SLE in patients with CHLE is approximately 18% so regular follow up with clinical/laboratory investigations to look for progression to SLE is very important.

Keywords: Chilblain, pernio, cutaneous lupus erythematosus, raynaud's phenomenon, CHLE

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:

Azib Shahid MD

Affiliation: Rosalind Franklin University, North Chicago, Illinois

Address: 2537 Meridian Drive, Great Lakes, Illinois, 60088

Tel: 773-822-8617

Email: azibshahid@gmail.com

References:

- 1) Hutchinson J. Harveian Lectures on Lupus. Br Med J. 1888 Jan 14;1(1411):58-63.
- 2) Hedrich CM, Fiebig B, Hauck FH, et al. Chilblain lupus erythematosus--a review of literature. Clin Rheumatol. 2008 Aug;27(8):949-954.
- 3) Viguier M, Piquier L, Cavelier-Balloy B, et al. Clinical and histopathologic features and immunologic variables in patients with severe chilblains. A study of the relationship to lupus erythematosus. Medicine (Baltimore). 2001 May;80(3):180-188.
- 4) Doutre MS, Beylot C, Beylot J, et al. Chilblain lupus erythematosus: report of 15 cases. Dermatology. 1992;184(1):26-28.
- 5) Franceschini F, Calzavara-Pinton P, Quinzanini M, et al. Chilblain lupus erythematosus is associated with antibodies to SSA/Ro. Lupus. 1999;8(3):215-219.
- 6) Vera-Recabarren MA, Garcia-Carrasco M, Ramos-Casals M, et al. Cutaneous lupus erythematosus: clinical and immunological study of 308 patients stratified by gender. Clin Exp Dermatol. 2010 Oct;35(7):729-735.
- 7) Millard LG, Rowell NR. Chilblain lupus erythematosus (Hutchinson). A clinical and laboratory study of 17 patients. Br J Dermatol. 1978 May;98(5):497-506.
- 8) Su WP, Perniciaro C, Rogers RS 3rd, et al. Chilblain lupus erythematosus (lupus pernio): clinical review of the Mayo Clinic experience and proposal of diagnostic criteria. Cutis. 1994 Dec;54(6):395-399.

- 9) Boada A, Bielsa I, Fernandez-Figueras MT, et al. Perniosis: Clinical and Histopathological Analysis. *Am J Dermatopathol*. 2010 Feb;32(1):19-23.
- 10) Lavigne C, Mailot F, Machet L, et al. Lethal pancytopenia associated with chilblain lupus erythematosus. *Acta Derm Venereol*. 2000 Sep-Oct;80(5):393.
- 11) Stainforth J, Goodfield MJ, Taylor PV. Pregnancy-induced chilblain lupus erythematosus. *Clin Exp Dermatol*. 1993 Sep;18(5):449-451.
- 12) Marks R, Baker H, Marten RH, et al. Chilblain lupus erythematosus as a manifestation of lymphoma. *Proc R Soc Med*. 1967 May; 60(5):494-496
- 13) Kelly JW, Dowling JP. Pernio. A possible association with chronic myelomonocytic leukemia. *Arch Dermatol*. 1985 Aug;121(8):1048-1052.
- 14) White KP, Rothe MJ, Milanese A, et al.. Perniosis in association with anorexia nervosa. *Pediatr Dermatol*. 1994 Mar;11(1):1-5.
- 15) Belizna CC, Tron F, Joly P, et al. Outcome of essential cryofibrinogenaemia in a series of 61 patients. *Rheumatology (Oxford)* 2008 Feb;47(2):205-207
- 16) Cribier B, Djeridi N, Peltre B, et al.. A histologic and immunohistochemical study of chilblains. *J Am Acad Dermatol*. 2001 Dec;45(6):924-929.
- 17) Rustin MH, Newton JA, Smith NP et al. The treatment of chilblains with nifedipine: the results of a pilot study, a double-blind placebo-controlled randomized study and a long-term open trial. *Br J Dermatol*. 1989 Feb;120(2):267-275.