

Case 19

A 50 year-old Thai woman from Roi-et

Chief complaint: Asymptomatic polymorphic skin eruptions for 4 weeks

Present illness:

The patient developed asymptomatic erythematous papules on both legs for 4 weeks. The lesions rapidly increased in number and expanded over the entire body before turning into central hemorrhagic crusts. She had no fever or any other illness that preceded the onset of her skin eruption. She denied recent medicine ingestions

Past history:

Diabetes mellitus and dyslipidemia treated with glipizide 10 mg/day, metformin 2000 mg/day and simvastatin 20 mg/day.

Family History:

Her family history was unremarkable for a similar skin eruption.

Physical examination:

HEENT: Not pale, no jaundice

Lymph nodes: Not palpable

Heart: Normal S1S2, no murmur

Lungs: Clear

Abdomen: Soft, no hepatosplenomegaly

Extremities: No pitting edema

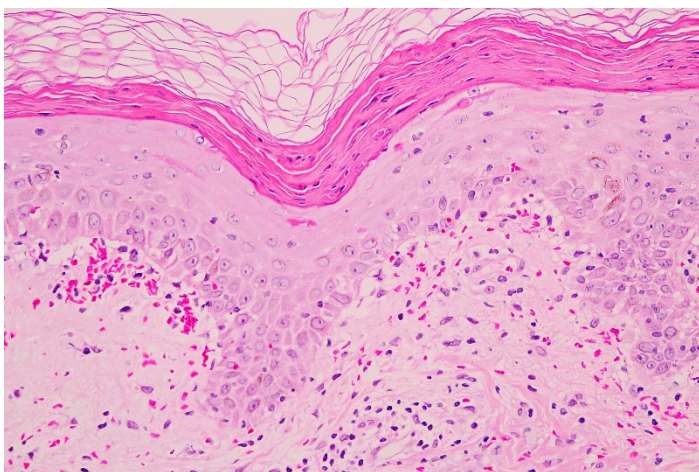
Skin examination:

- Generalized erythematous round to oval macules and papules, some lesions covered with superficial erosion with central hemorrhagic crust distributed all over the body.



Histopathology: (S16-21667A, Left forearm)

- Diffused parakeratosis, hypogranulosis, scattered necrotic keratinocytes and epidermal pallor.
- Superficial and deep perivascular inflammatory-cell infiltrate of lymphocytes and extravasated erythrocytes with some exocytosis.



Diagnosis: Pityriasis lichenoides et varioliformis acuta

Investigation:

CBC: WBC 10,260 (N 67%, L 26%, Mo 5%, Eo 1%, Ba 1%)
LFT: AST/ALT 20/26 U/L, ALP/GGT 112/34 U/L, DB/TB 0.2/0.5 mg/dL
FBS: 155 mg/dL
HbA1c 8.82%
BUN/Cr: 8/0.63 mg/dL
Viral hepatitis profile, anti HIV: Negative
CXR: No pulmonary infiltration

Treatment:

Oral methotrexate (2.5 mg) 2 tabs oral weekly
Doxycycline (100 mg) 1tab oral BID
Prednisolone 30 mg/day * 1 week and tapered off
0.1% TA milk lotion applied lesions BID

Presenter: Thirawut Sirikham, MD

Consultant: Pamela Chayavichitsilp, MD

Discussion:

Pityriasis lichenoides (PL) is an inflammatory skin disorder of unknown etiology, characterized by a self-limited skin eruption seen in either acute or chronic form with a variable clinical spectrum. Mucha was first to separate the acute form of PL from the chronic form in 1916. Later, in 1966, Degos *et al* described an ulceronecrotic variant of acute PL associated with fever, which was named Febrile Ulceronecrotic Mucha-Habermann disease.¹

Currently 3 subtypes of this spectral disease are recognized: pityriasis lichenoides et varioliformis acuta (PLEVA), pityriasis lichenoides chronica (PLC) and febrile ulceronecrotic Mucha-Habermann disease. PLC is 6 times more common than PLEVA.¹ PL affects children and young adults, peaking in the third decade of life.¹ Men are 3 times more likely to be affected than women.¹

The incidence and prevalence of the acute form of PL or pityriasis lichenoides et varioliformis acuta (PLEVA) are not well documented.

No specific risk factors, racial or geographic predisposition have been associated with PLEVA. PLEVA occurs in all age groups, but is found most frequently in patients in the second or third decades of life.² The disease tends to be slightly more frequent in men. It is not uncommon in children, but has been described in infants.³

The etiology of PLEVA remains unknown, although it has been described as lymphoproliferative in nature.⁴ Several theories have been proposed to explain its etiology, suggesting that it may be an inflammatory reaction triggered by infectious agents, an inflammatory response secondary to a T-cell dyscrasia, or an immune complex mediated hypersensitivity.⁵ Specific pathogens that have been proposed as a cause of PLEVA include adenoviruses, Epstein–Barr virus, *Toxoplasma gondii*, parvovirus B19, *Staphylococcus aureus*, and *Streptococcus pyogenes*.⁶ In addition to illnesses, such as upper respiratory tract infections, varicella, viral gastroenteritis and streptococcal pharyngitis, PLEVA has rarely been reported in association with rheumatic disease in children, influenza vaccination and premature labor and premature rupture of the membranes in pregnancies.^{1,6,7,8,9}

Clinically, PLEVA presents as asymptomatic crops of erythematous macules and papules in various stages of development that can become hemorrhagic, pustular or, necrotic. Lesions begin as 2-3 mm erythematous macules which rapidly develop into papules with progressively thickened fine scales, which characteristically present side by side, an important diagnostic sign. They usually occur on the trunk and flexural areas of the extremities, but generalized eruptions may occur.⁵ During the course of the disease, patients rarely have systemic signs or symptoms. Lesions typically leave little or no scarring; however, varioliform scars with post inflammatory hyperpigmentation or hypopigmentation may occur.^{5,10}

Febrile ulcerative PLEVA, or febrile ulceronecrotic of Mucha–Haberman disease (FUMHD), is a fulminant and potentially lethal variant of PLEVA. FUMHD is characterized by high fever, severe ulceronecrotic skin lesions with systemic involvement including

interstitial pneumonitis, abdominal pain, malabsorption, central nervous system and rheumatologic symptoms.⁶

PLEVA is often a clinical diagnosis, but characteristic histopathological findings confirm the diagnosis. It is characterized by a vacuolar interface dermatitis with a wedge-shaped superficial and deep perivascular lymphocytic infiltrate and transepidermal extravasation of erythrocytes. Necrotic keratinocytes, vesiculation, and ulceration may be seen in the epidermis. In PLC, epidermal changes are less prominent, the lymphocytic infiltrate tends to be more sparse with mild vacuolar changes at the dermo-epidermal junction.¹¹ In term of laboratory abnormalities, there have been several reports of patients presenting with a high erythrocyte sedimentation rate.¹²

Dermoscopic examination of PLEVA reveals papules with a central whitish patch and crusted lesions with an amorphous brownish structure. Both types of lesion are surrounded by a well-defined ring of pinpoint and/or linear vascular structures with a targetoid appearance. At higher magnification, the ring of vascular structures appeared dilated and convoluted, with some showing a glomerular pattern or linear arrangement and non-blanchable reddish globules. The vascular pattern seen under dermoscopy correlates with the presence of dilation and engorgement of blood vessels and microhemorrhages in the papillary dermis.¹³

Immunohistochemistry is useful in the diagnosis of PLEVA. In PLEVA, CD8+ cytotoxic T cells usually predominate over CD4+ cells in the dermal infiltrate and seem to mediate the more severe vascular damage and epidermal necrosis. Conversely, the lesions of PLC display fewer CD8+ cells in the infiltrate with less marked vascular and epidermal injury than those in PLEVA.¹⁴ Lymphomatoid papulosis which shares clinical features with PLEVA, can be distinguished by CD30 positivity.²

The differential diagnosis of PLEVA includes lymphomatoid papulosis (the condition most commonly mistaken for PLEVA),

arthropod bite reactions, varicella, Gianotti–Crosti syndrome, erythema multiforme, pityriasis rosea, guttate psoriasis, vasculitis, and secondary syphilis.^{2,6}

In terms of prognosis, PLEVA is typically benign and self-limiting which generally lasts over weeks to months however, in some cases can remain for years.^{5,15} Generalized PLEVA resolves two to three times more rapidly than localized PLEVA.¹⁶ PLEVA may transition into the chronic form or PLC, a process that may persist for years with frequent recurrences.¹⁵ Children have worse prognosis than adults, as they are less likely to experience remission, more likely to be left with post-inflammatory hyper- or hypopigmentation¹⁷, and often do not respond as well to treatment.²

PLEVA may be challenging to treat. Frequent spontaneous remission of the disease makes it difficult to evaluate the efficacy of pharmacologic intervention.² There are several therapeutic modalities ranging from natural ultraviolet light exposure to chemotherapeutic agents.⁵ Tetracycline is often administered to adults, but oral erythromycin is the drug of choice for pediatric patients.⁷ Recently, treatment of PLEVA with azithromycin have proven to be more effective because of greater adherence with its daily pulsed dosing (5 days every 2 weeks) compared to ongoing two to three times per day dosing with erythromycin. Moreover, azithromycin is associated with fewer gastrointestinal side effects than erythromycin.¹¹ Topical corticosteroids and systemic antihistamines may be administered for symptomatic relief of pruritus, but these medications do not alter the course of the disease.¹⁵ Topical immunomodulators, such as tacrolimus, may also be used.⁵ Psoralen plus ultraviolet A (PUVA) and ultraviolet B (UVB) phototherapy can be used as second-line therapies.⁵ Ongoing PUVA, UVA, and UVB are specifically useful in preventing relapse.¹⁵ However, the long-term risks of phototherapy in children remain unclear.⁷ Third-line therapies, such as methotrexate, acitretin,

dapsone, or cyclosporine, may be reserved for resistant or severe disease.⁵

Our patient was initially treated with topical corticosteroids and doxycycline 200 mg/day orally for 2 weeks with no improvement. We then started oral methotrexate 5 mg/week, oral prednisolone 30 mg/day and continued oral doxycycline 200 mg/day for 4 weeks. She was also offered UVB phototherapy but denied. She responded well to medical therapy with most lesions resolved leaving post-inflammatory hyperpigmentation as a result.

References

1. Castro BAC, Pereira JMM, Meyer RLB, Trindade FM, Pedrosa MS, Piancastelli ACC. Pityriasis lichenoides et varioliformis acuta after influenza vaccine—Case Report. *An Bras Dermatol* 2015;90:181-4.
2. Fernandes NF, Rozdeba PJ, Schwartz RA, Kihiczak G, Lambert WC. Pityriasis lichenoides et varioliformis acuta: a disease spectrum. *Int J of Dermatol* 2010;49:257–61.
3. Hoshina D, Akiyama M, Hamasaka K, Shimizu H. An infantile case of pityriasis lichenoides et varioliformis acuta. *Br J Dermatol* 2007; 157:194–6.
4. Weinberg J, Kristal L, Chooback L, Honig PJ, Kramer EM, Lessin SR. The clonal nature of pityriasis lichenoides. *Arch Dermatol* 2002;138:1063–7.
5. Bowers S, Warsaw EM. Pityriasis lichenoides and its subtypes. *J Am Acad Dermatol* 2006;55:557–72.
6. Tsianakas A, Hoeger PH. Transition of pityriasis lichenoides et varioliformis acuta to febrile ulceronecrotic Mucha–Habermann disease is associated with elevated serum tumour necrosis factor- α . *Br J Dermatol* 2005;152:794–9.
7. Ersoy-Evans S, Greco MF, Mancini AJ, Subasxi N, MD, Paller AS. Pityriasis lichenoides in childhood: A retrospective review of 124 patients. *J Am Acad Dermatol* 2007;56:205-10.
8. Eskandar M. Pityriasis lichenoides et varioliformis acuta in pregnancy. *Saudi Med J* 2001;22:1127–9.

9. Ellsworth J, Cassidy JT, Ragsdale CG, Sullivan DB. Mucha–Habermann disease in children – the association with rheumatic diseases. *J Rheumatol* 1982;9:319–24.
10. Miyamoto T, Takayama N, Kitada S, Hagari Y, Mihara M. Febrile ulceronecrotic Mucha–Habermann disease: a case report and a review of the literature. *J Clin Pathol* 2003;56:795–7.
11. Geller L, Antonov NK, Lauren CT, Morel KD, Garzon MD. Pityriasis Lichenoides in Childhood: Review of Clinical Presentation and Treatment Options. *Pediatr Dermatol* 2005;32:579–92.
12. Garcia B, Connelly EA, Newbury R, Friedlander SF. Pityriasis lichenoides and idiopathic thrombocytopenic purpura in a young girl. *Pediatr Dermatol* 2006;23:21–3.
13. Lacarrubba F, Micali G. Dermoscopy of Pityriasis Lichenoides et Varioliformis Acuta. *Arch Dermatol* 2010;46:1322.
14. Vonderheid EC, Kadin ME, Gocke CD. Lymphomatoid Papulosis Followed by Pityriasis Lichenoides: A Common Pathogenesis. *Am J Dermatopathol* 2011;33:835–40.
15. Patel D, Kihiczak G, Schwartz RA. Pityriasis lichenoides. *Cutis* 2000;65:17–23.
16. Tilly J, Drolet BA, Esterly NB. Lichenoid eruptions in children. *J Am Acad Dermatol* 2004;51:606–24.
17. Ellerbroek V, Hamm H. Pityriasis Lichenoides et Varioliformis Acuta: Remission with Hypopigmentation. *J Pediatr* 2016;11:331–6.