PLEVA in an Adult Patient with an Unclear HSV Association

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Abstract
Pityriasis lichenoides et varioliformis acuta (PLEVA) is a rare clonal T-cell disorder typically affecting pediatric patients. It is characterized by an acute, self-resolving pleomorphic cutaneous eruption with an unpredictable relapsing and remitting clinical course. PLEVA has been associated with various infections and medications. We report the case of a young, otherwise healthy, adult female with PLEVA.

Case Report
A 22-year-old female presented with a two-week history of a worsening acute, pruritic and slightly “burning” rash all over her body. She had seen her primary care physician twice at referral, initially when the rash was confined to her upper chest, and was placed on oral clindamycin. She returned when the rash continued to spread. Bacterial cultures yielded coagulase-negative staphylococcus, and she was given oral methylprednisolone taper and oral doxycycline.

She had a past medical history of attention deficit disorder and depressive/anxiety disorder. Her current medications included an oral contraceptive pill that she restarted after the rash appeared, escitalopram oxalate 10 mg daily, and methylphenidate 10 mg twice daily. She had no recent medicine change prior to the eruption. Possible contact allergens were not applicable or relevant.

Physical examination revealed an impressive varicelliform dermatitis affecting the symmetric bilateral chest, abdomen, upper and lower back, buttocks, groin, thighs, upper arms, and tapering out onto the distal upper and lower extremities. She had subtle facial involvement, but her scalp, palms, soles, nails and mucous membranes were spared. There was no palpable lymphadenopathy.

The cutaneous lesions were numerous with multiple stages of evolution present, consisting of oval-shaped pink macules and papules, some with central dusky coloration and superficial scale (Figures 1a, 1b). Other lesions had eroded surfaces with hemorrhagic crusting (Figure 1c). The lesions were concentrated centrally, with relative sparing of acral sites, and tended to follow Langer’s lines (Figure 1d), favoring an endogenous etiology. There were admixed hyper- and hypopigmented macules where previous lesions had resolved, yielding an overall mottled appearance. Our differential diagnosis at this point included PLEVA, lymphomatoid papulosis, erythema multiforme, drug eruption, varicella, and other viral exanthems.

Routine labs, including a complete blood count with differential and a complete metabolic panel, were unremarkable. Varicella zoster virus (VZV) antibody titers revealed negative immunoglobulin M (IgM) and elevated immunoglobulin G (IgG). Herpes simplex virus (HSV) IgG antibody titers were negative, but HSV IgM titers were positive. She denied any current or prior symptoms or signs consistent with oral or genital herpes simplex or zoster.

Histologic findings revealed a basket-weave orthokeratosis with focal parakeratosis and red-blood-cell exocytosis overlying diffuse basal vacuolization with underlying patchy lymphocytic infiltration, consistent with a diagnosis of PLEVA (Figure 2).
At that time, additional lab tests were performed in order to rule out possible underlying etiologies. The following were negative: anti-streptolysin O antibodies, western blot for HIV-1 and -2, rapid plasma reagin test, toxoplasma IgM and IgG antibodies, hepatitis C virus (HCV) antibody screen, hepatitis B virus (HBV) core and surface antibodies and surface antigen, and heterophile antibody test. Epstein-Barr virus (EBV) screening panel revealed positive nuclear antigen and viral capsid antigen IgG antibodies, but negative viral capsid antigen IgM and early antigen IgG.

At her initial visit, we recommended completion of her course of doxycycline due to possible secondary infection. Triamcinolone 0.1% cream twice daily for two weeks, over-the-counter oral loratadine 10 mg twice daily, and over-the-counter oral diphenhydramine 25 mg at bedtime were prescribed for and provided symptomatic relief. After histologic confirmation of the diagnosis, we checked a beta human chorionic gonadotropin test, which was negative, and low-dose methotrexate was initiated at 7.5 mg weekly. Due to the presence of elevated HSV IgM antibodies, we recommended the patient complete a 10-day course of valacyclovir 1 gram twice daily, though the patient was still asymptomatic.

At one month follow-up, the patient reported no new lesions in the past two to three weeks, and the vast majority of the lesions were resolving with residual post-inflammatory hypopigmentation (Figure 3). The patient will be maintained on methotrexate 7.5 mg weekly until all lesions have resolved. The patient moved away, so HSV IgM and IgG labs were not repeated and there has been no long-term follow-up to date.

Discussion

Pityriasis lichenoides et varioliformis acuta (PLEVA), also known as Mucha-Habermann disease, is a rare disease on one side of a continuum with pityriasis lichenoides chronica (PLC), both in the family of clonal T-cell disorders. Mucha first identified the acute form of pityriasis lichenoides in 1916. Habermann coined the phrase PLEVA in 1925.6 The number of cases and the extent of PLEVA have not been well documented.1 Incidence and prevalence seems to be increased in the fall and winter months, among males, and during the second and third decades of life.7

Though exact etiology is unknown, evidence suggests PLEVA is a T-cell dyscrasia or an immune-complex-mediated hypersensitivity reaction to an infectious agent or drug.1 Postulated associations include: HIV, viral hepatitis, EBV, HSV, toxoplasma, TNF-a inhibitors, radioccontrast dyes, estrogen-progesterone, and the measles vaccine.2,8-12 While both PLEVA and PLC contain lesional T-cell infiltrates, CD8+ cells predominate in PLEVA, and CD4+ cells predominate in PLC.

The disease begins with an acute, diffuse eruption of erythematous macules and papules that rapidly evolve into crusted papules, vesicles, pustules and ulcers with various stages all present simultaneously.13-16 Lesions are approximately 2 mm to 10 mm in diameter, arranged singly or in clusters, most commonly on the trunk, medial extremities, and flexor surfaces.1,7 Patients with PLEVA are usually asymptomatic, but lesions may be pruritic or burn. While typically confined to the skin, patients may experience malaise, low-grade fever, lymphadenopathy, or rarely more serious complications like arthritis, superinfection, or bacteremia. A severe variant termed "febrile ulceronecrotic Mucha-Habermann disease" (FUMHD) may also involve the mucosa, gastrointestinal and pulmonary systems.8 Lesions may spontaneously resolve within weeks to months, or follow a more unpredictable relapsing and remitting course. Residual varioliform scars and inflammatory hyper- or hypopigmentation may be seen.1

The differential diagnoses for PLEVA include: lymphomatoid papulosis, cutaneous small-vessel vasculitis, drug eruption, arthropod reaction, viral exanthems, folliculitis, erythema multiforme, and dermatitis herpetiformis.1,17-21 Cutaneous biopsy is the gold-standard diagnostic test. Classic histologic findings of PLEVA are perivascular lymphocytic infiltrates, interface dermatitis with necrotic keratinocytes, and erythrocyte extravasation.2 Other testing may be helpful in excluding alternate diagnoses and uncovering underlying etiologies, but are generally not necessary to diagnose PLEVA.

The majority of treatment options for PLEVA are based on uncontrolled trials, case reports, and anecdotes. Tetracycline in adults or erythromycin in children are prescribed first-line treatments for their anti-inflammatory properties, often requiring a prolonged course followed by a gradual taper.2 Phototherapy is also effective, especially in relapsing disease, but the risk-benefit analysis of UV exposure is unclear.17 Cases with a rapid onset may warrant low-dose weekly methotrexate. Combination therapy (e.g., erythromycin with psoralen + ultraviolet A phototherapy [PUVA] or methotrexate with PUVA) is also effective. Other antibiotics may be used for superinfection. Topical corticosteroids, topical coal tar, and systemic antihistamines have been used for symptomatic relief.17 Systemic corticosteroids should be reserved for cases with systemic symptoms. Severe cases may require immune-suppressing and immune-modulating medications like tacrolimus and cyclosporine once infection has been excluded.22 The prognosis for PLEVA is generally good. Patients with diffuse involvement typically experience resolution faster than those with localized involvement.16 Pediatric patients are less likely to go into remission, are more likely to have permanent skin damage, and often do not respond to treatment as well as adults.7 Predisposition toward developing T-cell lymphoma is controversial.2

A literature search revealed a very limited number of previous cases of PLC and FUMHC associated with HSV infection, but no cases of
The connection between HSV and PLEVA was examined due to the obscurity of the association in the literature. In both cited case reports, the patients had active HSV lesions that coincided with their pityriasis lichenoides eruptions. The active lesions tested positive for HSV. Both cases were successfully treated with an antiviral (acyclovir).

**Conclusion**

PLEVA is a rare disorder, usually self-limited, but carries an unpredictable course. It is grossly characterized by pleomorphic lesions at various stages of evolution, and histologically as an interface dermatitis consisting of CD8+ T cells with extravasated erythrocytes. PLEVA has been associated with several infections and medications and has many proposed treatments. We report the case of a young, otherwise healthy adult female who was found to have a positive HSV IgM titer. This may or may not have been a coincidence, since repeat HSV studies were not done. Our patient was lost to follow-up, so there was no long-term surveillance for recurrence.

**References**


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