Pityriasis Lichenoides et Varioliformis Acuta in Adult Woman with Asymptomatic Bacteriuria: Another Possible Trigger?

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Abstract

Introduction*: Pityriasis Lichenoides et Varioliformis Acute (PLEVA) is a rare and benign inflammatory skin disease. This acute form is distinguished from the milder chronic condition, Pityriasis Lichenoides Chronica (PLC). The etiology of PLEVA itself remains unclear, although it has been associated with infection as a trigger.*
Case*: Here, we present the case of a 34-year-old woman who presented with abrupt, generalized, pruritic skin eruptions for two months.*
Case Discussion*: The eruptions started as red scaly papules and vesicles and resolved as hyperpigmentations. She denied having any previous dermatological diseases, routine medications, or vaccinations. On examination, she showed generalized multiple hyperpigmented macules, scaly papules, and vesicles over the trunk, extremities, and face, with erosions and crusts in several areas. Eosinophilia and asymptomatic bacteria were found in her urinalysis. A skin biopsy showed diffuse lymphocytic infiltration in the dermal/epidermal junction and perivascular region, with parakeratosis and lymphocyte exocytosis. While the pathogenesis of PLEVA itself remains unclear, a triggering factor of inflammatory reaction, such as infection, may contribute to the development of the disease.*
Conclusion*: Asymptomatic bacteriuria is associated with inflammatory responses, and thus, it can be one of many possibilities. More studies are needed to confirm this association with PLEVA. Due to the lack of a clear pathogenesis and the benign nature of the disease, this rare entity may present difficulties in diagnosis and therapy*

Keywords: *Pityriasis lichenoides et varioliformis acuta, PLEVA, Asymptomatic bacteriuria*

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Pityriasis Lichenoides et Varioliformis Acuta pada Wanita Dewasa dengan Bakteriuria Asimptomatik: Sebuah Pemicu Lain?

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Abstrak

***Pendahuluan**: Pityriasis Lichenoides et Varioliformis Acute (PLEVA) adalah penyakit inflamasi akut pada kulit yang jinak dan jarang terjadi. Etiologi PLEVA masih belum jelas, namun beberapa kondisi sering diidentifikasi sebagai pemicu.*
***Laporan Kasus**: Dalam tulisan ini, kami melaporkan kasus seorang wanita berusia 34 tahun dengan erupsi kulit yang gatal dan muncul tiba-tiba pada hampir seluruh area tubuh selama 2 bulan.*
***Diskusi**: Lesi kulit awalnya berupa papula eritematosa bersisik, kemudian berkembang menjadi vesikel dan erosi, dan akhirnya menjadi lesi hiperpigmentasi. Pasien tidak memiliki riwayat penyakit kulit sebelumnya, tidak mengonsumsi obat rutin, dan tidak mendapatkan vaksinasi saat lesi kulit pertama kali muncul. Pada pemeriksaan fisik, ditemukan lesi makula hiperpigmentasi multipel, makula bersisik, dan vesikel yang disertai erosi dan krusta pada punggung, ekstremitas, dan wajah. Pada pemeriksaan darah terdapat eosinofilia dan pada hasil urinalisis ditemukan bakteri. Hasil biopsi kulit menunjukkan adanya parakeratosis, infiltrat limfosit pada perivaskuler dan dermal/epidermal junction, serta eksositosis limfosit.*
***Kesimpulan**: Bakteriuria asimtomatik dapat mencetuskan reaksi inflamasi, yang mana dapat berakibat menjadi PLEVA pada kasus ini. Namun, diperlukan penelitian lebih lanjut untuk mengonfirmasi hubungan antara bakteriuria asimtomatik dengan kejadian PLEVA. Karena etiologi yang belum jelas dan sifat penyakit yang jinak, PLEVA dapat menyulitkan dalam diagnosis dan pengobatan.*

***Kata Kunci:** Pityriasis lichenoides et varioliformis acuta, PLEVA, Bakteriuria asimtomatik*

Introduction

Pityriasis lichenoides (PL) is a rare and benign skin inflammatory disease characterized by scaly papules that can progress into erosions and crusts. The lesions are initially red-brown spots that resolve into hyperpigmentations.[1] PL can present in two forms: an acute form known as pityriasis lichenoides et varioliformis acuta (PLEVA) and a mild chronic form called pityriasis lichenoides chronica (PLC).[2] The etiology of PL is still unknown, but it is often associated with inflammation triggered by infection, hypersensitivity, or T-cell dyscrasia. Here, we report a case of PLEVA in a 34-year-old woman that may have been triggered by asymptomatic bacteriuria."

Case

A 34-year-old woman presented with a 2-month history of abrupt, generalized, pruritic skin eruptions over her trunk, face, and extremities. The eruptions were first recognized as erythematous papules and vesicles that developed into erosions and ulcers, and resolved as hyperpigmented patches. She had no history of chronic illnesses, allergies, recent blood transfusions, or vaccinations. She did not have any pets and had no recent travel history. Neither she nor her relatives had previous episodes of similar symptoms or other dermatologic diseases.

She was stable and afebrile. Dermatological examination revealed multiple generalized erythematous and hyperpigmented

macules, plaques with scaling, vesicles, erosions, and excoriations with hemorrhagic crusts (Figure 1a-f). Lesions were primarily found on the trunk and extremities and on the facial area, while mucous membranes were spared. No palpable lymph nodes were noted. The hematological panel showed a leukocyte count of 9,130 cells/uL with 6% eosinophils, and an eosinophil count of 710 cells/uL. The ANA profile was within normal limits. A complete urinalysis panel showed positive leucocyte esterase, leukocyturia of 19 cells/uL, and bacteriuria (+1). Her skin biopsy revealed diffuse lymphocytic infiltration in the dermal/epidermal junction and perivascular area, parakeratosis without hyperkeratosis, and lymphocytic exocytosis, which are consistent with pityriasis lichenoides et varioliformis acuta (PLEVA) (Figure 2-6).

The patient had previously received oral methylprednisolone 16 mg three times a day (tid) along with clobetasol propionate 0.05% cream and mupirocin cream. After three weeks of treatment, there was no improvement, and new lesions continued to appear. The treatment was stopped, and another treatment was initiated. She was treated with erythromycin 500 mg tid, methylprednisolone 4 mg tid, loratadine 10 mg once daily (od), and vitamin D3 1,000 IU twice a day (bid) for 14 days. The patient was scheduled for weekly evaluation. After two weeks, the patient showed significant improvement as her lesions dried up without any new active lesions and became less pruritic.

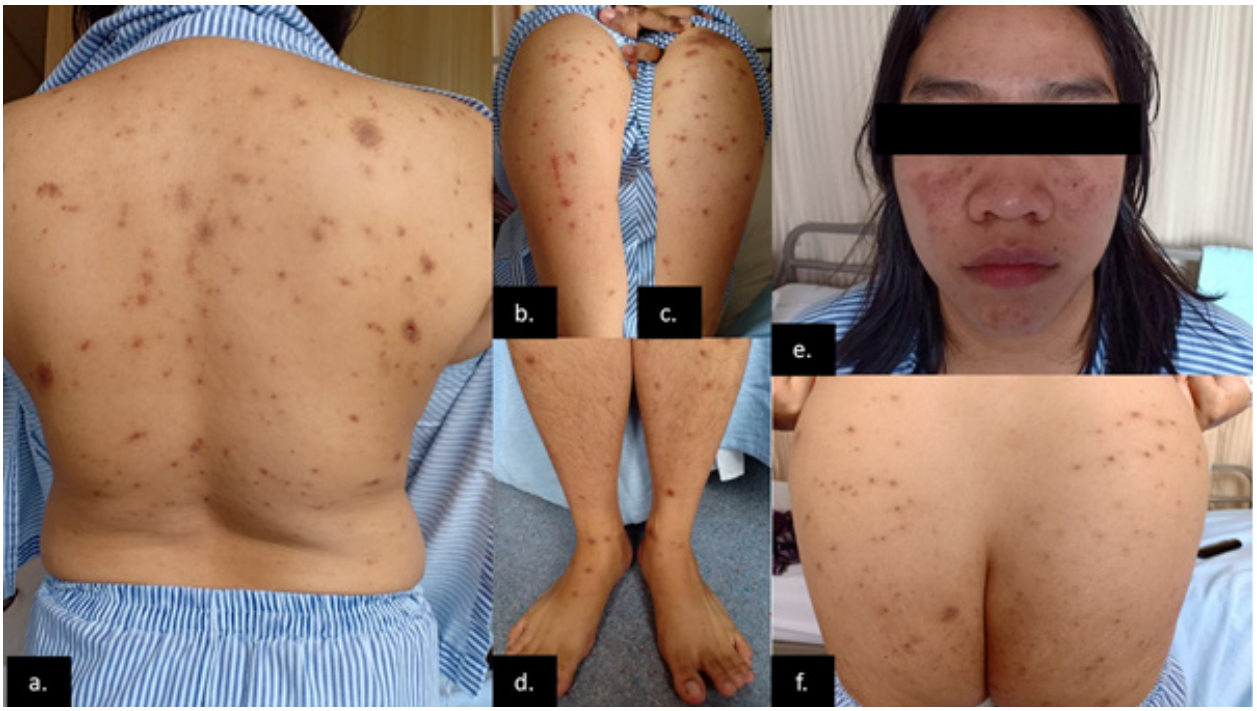

Figure 1. (a. - f.) Generalized multiple erythematous and hyperpigmented macules, plaques with scaling, vesicles, erosions and excoriations with haemorrhagic crusts on the trunk, extremities, and facial area

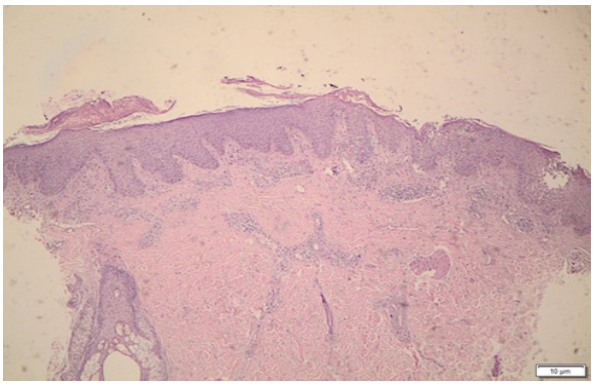

Figure 2. Diffuse lymphocytic infiltration in the dermal/epidermal junction (10x magnification)

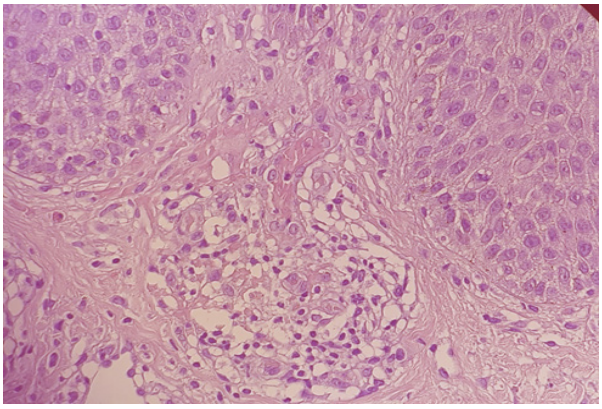

Figure 3. Diffuse lymphocytic infiltration in the dermal/epidermal junction (40x magnification)

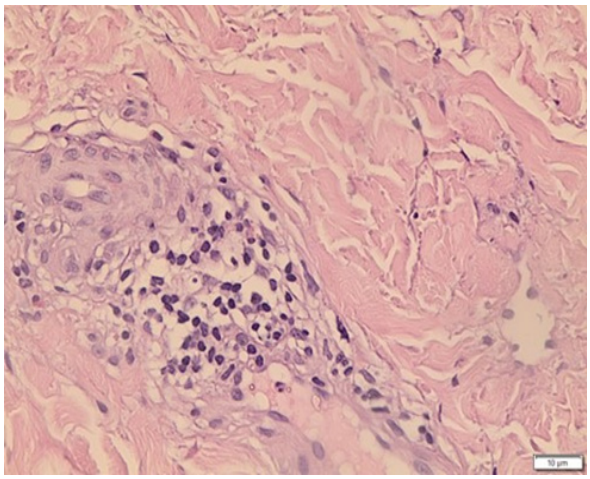

Figure 4. Lymphocyte infiltration around perivascular area (40x magnification)

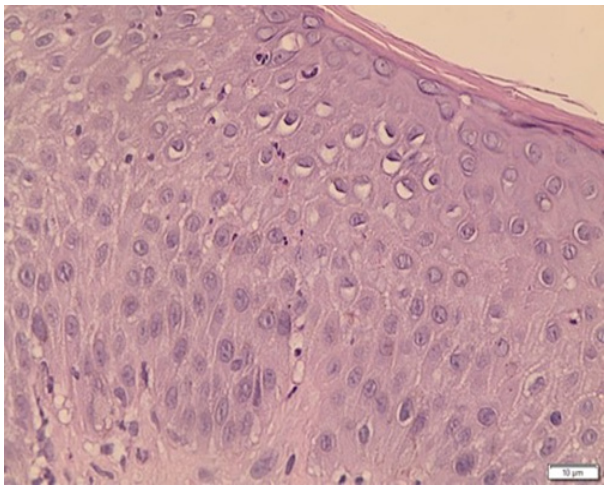

Figure 6. Exocytosis of the lymphocytes at the epidermal area (40x magnification)

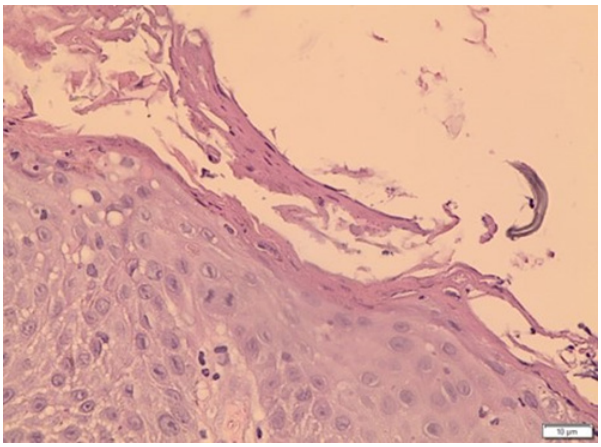

Figure 5. Parakeratotic process without hyperkeratosis at the epidermal area (40x magnification)

Case Discussion

In 1894, Neisser and Jadassohn described pityriasis lichenoides (PL) as a spectrum of papulosquamous skin eruptions associated with parapsoriasis.[1] The chronic variant, known as pityriasis lichenoides chronica (PLC), is three to six times more common than the acute variant, pityriasis lichenoides et varioliformis acuta (PLEVA), or Mucha-Habermann disease (MHD). PLEVA can occur at any age but is more frequent in children and young adults under 30 years old, with a higher incidence in males than females.[2] In this case, the patient was a 34-year-old female, which is outside the typical population for PLEVA.

The etiology of PLEVA remains unclear. However, several case reports link PLEVA with various infectious agents, such as Toxoplasma gondii, Epstein-Barr virus (EBV), Cytomegalovirus (CMV), Parvovirus B19, Human Herpes Virus 7 (HHV-7), Human Herpes Virus 8 (HHV-8), Human Immunodeficiency Virus (HIV), Staphylococcus aureus, and Group A Streptococcus beta-hemolyticus. Other case reports have also mentioned the manifestation of PLEVA after receiving estrogen-progesterone replacement therapy, cancer chemotherapy, and vaccination.[3,4] Thus, the pathogenesis of PLEVA is believed to be caused by one of three theories: an inflammatory reaction triggered by microorganism invasion, a benign T-cell lymphoproliferative process, or an immune complex-mediated vasculitis.[5]

PLEVA starts with multiple erythematous papule eruptions with a fine central scale that later becomes vesiculopustules with hemorrhagic necrosis, crusts, ulcers, and red-brown crusts. Although uncommon, these lesions can show with burning sensations, pruritus, or systemic symptoms. The lesions usually show in their predilective site, including the trunk and proximal area of the extremities, as seen in this patient. PLEVA can heal in several weeks or months without treatment, becoming post-inflammatory hyperpigmented or hypopigmented macules or varicella-like scars.[6,7]

It can be challenging for physicians to differentiate PLEVA from other common skin lesions due to its low prevalence. Lymphomatoid papulosis, which also presents with papule eruptions as initial lesions, is often confused with PLEVA. However, the eruptions in lymphomatoid papulosis tend to last for years and can develop into nodules, tumors, and plaques in the later stage, and are usually more significant and less numerous compared to PLEVA.[8] Arthropod bite reactions may also cause multiple, widespread, pruritic, inflammatory papules, but the skin lesions found in PLEVA are scaly, crusted, and distributed symmetrically on the trunk and limbs.[9] While

erythema multiforme and varicella can also be considered, they usually involve the mucous membranes. Nonetheless, a case report mentioned the coexistence of PLEVA and varicella by detecting Varicella-Zoster Virus through PCR from the skin sample.[10] Clinical history regarding exposure and vaccination for the varicella-zoster virus can help to elucidate the diagnosis. Histopathology is the gold standard to confirm a definite diagnosis of PLEVA.[11] Typical histopathological findings include infiltrations of inflammatory cells, mainly T-cell CD8+, at the basal layer of the dermis and perivascular area in early lesions, and lymphocyte exocytosis, hyperkeratosis, parakeratosis, and necrosis seen at the epidermal layer in late lesions.[6] Direct immunofluorescence study showed vascular and perivascular deposits of IgM, C3, and fibrin in the early lesion, which later become diffuse deposits of fibrin, albumin, and immunoglobulins in the epidermis and dermis in the advanced stage. The deposits of fibrin in the late skin lesions suggest extensive direct vascular injury by CD8+ cells with non-specific leakage of immunoreactants from vessels in association with nonspecific deposition of immunoreactants in areas of epidermal necrosis and ulceration. In lymphomatoid papulosis, histological findings are characterized by large atypical nonlymphoid cells, resembling Reed-Sternberg cells, with many neutrophils, few lymphocytes, almost no necrotic keratinocytes, and little vacuolar degeneration of the basal layer.[8]

Several immunopathological observations have been made regarding the proposed pathogenesis theories of PLEVA, which mainly involve the role of T-lymphocytes. The theory of PLEVA as a benign T-cell lymphoproliferative process remains controversial, as previous studies in 13 out of 20 patients have shown co-expression of CD8+ and CD30+. However, a two-and-a-half-year follow-up showed no evidence of lymphoid malignancy. Therefore, most studies correlate PLEVA with being triggered by an infectious agent. Interestingly, a study performed in Korea found a 100% detection rate of Human Herpes Virus in skin biopsies of patients with Kaposi Sarcoma, with a lower detection rate in peripheral blood. However, viral genomes in human keratinocytes are undetectable through polymerase chain reaction (PCR) 8 weeks after primary infection.[12–14]

The patient's diagnosis of PLEVA was confirmed by both the appearance of skin lesions and histopathological examination. However, the trigger for PLEVA in this patient is still unknown. It was challenging to identify risk factors for PLEVA, as the patient did not have any prodromal symptoms, drug consumption, previous similar episodes, or chronic disease. Additional tests could be helpful in ruling out similar diseases to PLEVA. Due to limited testing modalities, other infectious agents as triggers for skin lesions could not be ruled out. However, a complete urinalysis panel revealed that the patient had asymptomatic bacteriuria, which could potentially be the infectious trigger for skin inflammation.[8]

While no case reports have ever mentioned PLEVA after an asymptomatic urinary tract infection, asymptomatic bacteriuria has been associated with certain inflammatory reactions.[15,16] The inflammatory reaction in asymptomatic bacteriuria causes urothelial injury, mainly from a neutrophil-driven inflammatory response. Other mediators, such as leukotrienes B4 (LTB4) and C4 (LTC4), may also contribute to an inflammatory reaction, which is found in both asymptomatic bacteriuria and urinary tract infections (UTIs). Asymptomatic bacteriuria does not typically require treatment, except in pregnancy, hemodialysis, and kidney transplants.[15] A study about overtreatment in asymptomatic bacteria was conducted, and one of the reasons was due to elevated inflammatory markers.[17] A cohort study in asymptomatic bacteriuria found several cytokines, such as interleukin 8 (IL-8), Eotaxin-1, antibacterial peptide interferon-gamma-induced protein 10 (IP-10), and inflammatory regulators interleukin 1 (IL-1). Compared to symptomatic UTI, the level of IL-6 was low in asymptomatic bacteriuria.[18] One of the three theories of the pathogenesis of PLEVA is associated with microorganism invasion that leads to an inflammatory reaction, which may contribute in this case, where the patient had concomitant asymptomatic bacteriuria. However, further studies are needed to confirm the relationship between asymptomatic bacteriuria and the development of PLEVA. Within the inflammatory reaction, besides an extrinsic trigger, a reaction secondary to T-cell dyscrasia or hypersensitivity reaction may contribute as well.[19]

Although the etiology and pathogenesis of PLEVA remain uncertain, there is no established standardized treatment for this condition. The disease is self-limiting, making it difficult to evaluate the efficacy of any therapeutic modalities. Close monitoring without pharmacologic intervention may be sufficient to heal the lesions in some cases.[20] However,

tetracycline and erythromycin have shown promising benefits by inhibiting IL-6 and IL-8 gene expression and decreasing intercellular adhesion molecules. Different dosages of these drugs have been reported in the literature, with a minimum dose of 15-30 mg/kg/day for at least 10 days showing promising results without any reported side effects if used for 6 months. If there is no clinical improvement after 1.5 months, dose increment can be considered, with a medium treatment duration of 3 months. Recurrence can occur after drug discontinuation.[21] Topical corticosteroids and antihistamines are helpful in relieving symptoms in severe cases, but the disease course remains unaltered. In this case, the patient received oral erythromycin 500 mg tid for 14 days, and there was significant improvement after 2 weeks. The previous lesions had dried up, become less pruritic, and no new active lesions appeared. While corticosteroids are indicated for relief of irritation, they are not the first line of treatment for PLEVA, which is an autoimmune skin disorder.[22] In some cases, corticosteroids are not very effective in treating PLEVA, which raises concern for the diagnosis along with pathology examination.[23] Although PLEVA is a benign skin disorder, further studies are needed to determine its risk factors, triggering factors, such as asymptomatic bacteriuria in this case, and potential long-term complications for better prevention and management.

Conclusion

Pityriasis lichenoides et varioliformis acuta (PLEVA) is a rare skin condition in an adult woman. With a low prevalence of cases, a histopathological skin examination is required to confirm the definite diagnosis. Whenever the resources are available, the possible triggers to the inflammatory cascade in PLEVA must be evaluated with a series of further examinations. While there are not enough reports about asymptomatic bacteriuria as the causal factor in PLEVA, additional studies may be needed to confirm asymptomatic bacteriuria as one of many possibilities of triggering factors. Repeat urinalysis may be indicated if the patient develops another episode of PLEVA to confirm the association of it with asymptomatic bacteriuria. This rare, self-limiting entity may present difficulties in diagnosis and its triggering factor. Due to various disease progressions, no standard treatment for PLEVA has been established.

Ethics approval and consent to participate

The patient gave consent for this case report and photograph documentation to be published in a scientific journal without revealing her identity. The hospital's institutional review board approved for this case report publication in a scientific journal without revealing the patient's identity.

Consent for publication

Informed consent was obtained from the patient for publication of this case and accompanying images.

Availability of data and materials

Not applicable

Competing interests

None

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Authors' contributions

Theo Audi Yanto and Nana Novia Jayadi evaluated and treated the patient. Nathania Raphaeli Mulia performed data collection from the patient and her medical files. Theo Audi Yanto, Nathania Raphaeli Mulia, Abraham Fatah, and Nana Novia Jayadi drafted the manuscript. Nathania Raphaeli Mulia and Abraham Fatah performed data analysis and interpretation. Theo Audi Yanto and Nana Novia Jayadi supervised and gave expert advice regarding the manuscript. Theo Audi Yanto, Nathania Raphaeli Mulia, Abraham Fatah, and Nana Novia Jayadi gave the final approval of the version to be published.

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