Journal of Pakistan Association of Dermatologists. 2026;**36(2)**:322-326.

Case Report

When psoriasis isn't psoriasis: Psoriasiform syphilis and the hidden prozone phenomenon

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Abstract

Syphilis is a systemic infection that may present atypically in HIV patients and produce misleading serologic results, including the prozone phenomenon. A 25-year-old man with a history of sex with men presented with 3 months of weight loss and 3 weeks of generalized erythematous, scaly, psoriasiform plaques on the face, scalp, trunk, extremities, palms, soles, and penis, with painless penile ulcers and intermittent pruritus. The patient was newly diagnosed with HIV infection with severe immunosuppression (CD4 189 cells/µL). Initial RPR was nonreactive, but repeat testing with serum dilution became reactive (1:32), confirming a prozone effect**.** The TPHA was strongly reactive (1:2560). Skin biopsy showed psoriasiform hyperplasia with plasma cell-rich infiltrates, supporting psoriasiform secondary syphilis. Treatment with antiretroviral therapy and weekly benzathine penicillin G for three weeks led to clinical improvement and declining RPR titers. This case highlights recognition of atypical syphilis and the need to suspect prozone in HIV patients.

Article Received on 16.12.2025

Revised on 27.04.2026

Accepted on 11.05.2026

Published on 30.06.2026

Keywords Syphilis; Secondary syphilis; Psoriasiform syphilis; Prozone phenomenon.

Citation: Faidah I, Salamah F, Hidayati AN, Murtiastutik D, Widyantari S, Astindari, Agusni RI. When psoriasis isn't psoriasis: Psoriasiform syphilis and the hidden prozone phenomenon. *J Pak Assoc Dermatol*. 2026;**36(2)**:322-326.
Doi: https://doi.org/10.66344/jpad.v36i2.3301

Introduction

Treponema pallidum subsp. *pallidum*, often known as *T. pallidum* below, is the cause of syphilis, a systemic human illness that can be either acquired or congenital. Early and late syphilis are two types of acquired syphilis, which is primarily caused by sexual intercourse. Primary, secondary, and early latent syphilis are all considered forms of early syphilis. Late latent and tertiary syphilis are forms of late syphilis.[1]

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Syphilis is found all throughout the world and is more frequently observed in men having sex with men and rarely in children. The skin, mucosa, and other organ systems are all affected by syphilis. Transmission of syphilis occurs during sexual intercourse.[2] The incidence of primary and secondary syphilis rose by 22.7% in women and 14.4% in men between 2013 and 2014. Furthermore, between 2013 and 2017, the prevalence of syphilis almost doubled. According to epidemiological data from 2016, there were 7,055 cases of syphilis in Indonesia.[3]

Syphilis is one of the greatest imitator in dermatology. Psoriasiform syphilis, in which the lesions simulate psoriasis was a feature well appreciated by old Dermatologists and named as

syphilide psoriasiforme or psoriasis syphilitique. Psoriasiform syphilis is a rare presentation of secondary syphilis and may be seen as part of the great imitator in dermatology, skin physicians should recognize this condition to avoid mistreatment of patients affected with syphilis with immunosuppressive drugs.[4]

The prozone phenomenon is a recognized diagnostic pitfall in syphilis, particularly in patients with HIV coinfection and secondary-stage disease. It occurs when excessively high antibody titers interfere with antigen–antibody lattice formation in nontreponemal tests such as RPR or VDRL, resulting in false-negative or weakly reactive results.[5]

This report describes a case of psoriasiform syphilis presenting with HIV coinfection which demonstrated a false negative reaction to the serum rapid plasma reagin (RPR) test.

Case Report

A 25-year-old homosexual man from Surabaya presented to our outpatient clinic with a 3-month history of weight loss, and was confirmed to be HIV-naïve. The patient developed erythematous patches on the face and scalp, which progressively spread to the legs, hands, and eventually involved the entire body since 3 weeks. The lesions became dry, scaly, and pruritic, with intermittent itching. Painless sores appeared on the shaft of the penis, accompanied by reddish patches in the same area. The patient also reported associated hair loss. The patient denied any history of medication use, and there was no family history of psoriasis.

Physical examination disclosed no enlargement of lymph nodes. Dermatological examination on facial region, anterior and posterior colic regions, anterior and posterior thoracic regions, gluteal region, upper and inferior extremity regions revealed multiple well-defined erythematous papules, macules, and plaques, some confluent, with white scale, erosions, and minimal excoriation; on penile region revealed numerous macules sharply demarcated erythematosus, erosions are present; on the palms and soles revealed erythematous-squamous psoriasiform lesions **(Figure 1)**.

Figure 1 Dermatological examination of facial, back, upper and lower extremities, penile region revealed multiple well-defined erythematous papules, macules, and plaques, some confluent, with white scales, erosions, and minimal excoriation

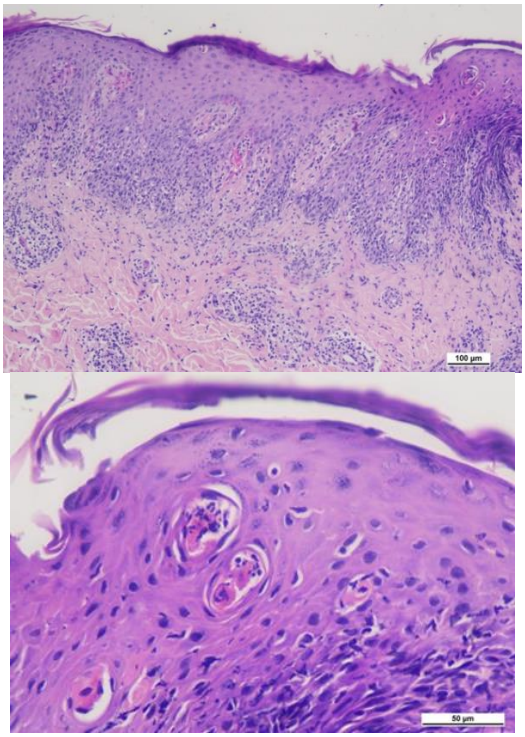

Figure 2 The histopathology showed psoriasiform epidermal hyperplasia with parakeratosis, irregular acanthosis, vacuolar basal degeneration, and a plasma cell-rich perivascular dermal infiltrate, without Munro microabscesses

Potassium hydroxide examination of the skin lesion revealed no fungal elements. Darkfield examination of the penile skin lesion revealed no *Treponema pallidum* visible.

Laboratory investigations disclosed a serologic diagnostic test for syphilis, RPR was nonreactive and TPHA was reactive with a titer of 1/2560. Repeat testing with serum dilution became reactive (1:32). Additional findings included reactive results of HIV three methods of serologic test with an CD4 absolute count of 189/mL and CD4% count of 7.90%.

Skin biopsy was performed on a lesion of the trunk to confirm the presumptive clinical diagnosis of psoriasis vulgaris **(Figure 2)**. The histopathology examination showed skin tissue section covered by epidermis with parakeratosis, irregular acanthosis, psoriasiform hyperplasia, dyskeratosis, moderate to severe spongiosis, and intraepidermal neutrophil infiltration. Vacuolar degeneration of basal cells was also visible. No Munro microabscesses were visible. Several plasma cells and perivascular lymphocytes were visible in the dermis.

The diagnosis of psoriasiform secondary syphilis with HIV infection was established based on the clinical presentation of erythematous scaly plaques mimicking psoriasis, with an atypical distribution not consistent with classic psoriasis and the presence of characteristic lesions on the dorsum of the penis. Serological testing revealed a reactive HIV, TPHA result, and the RPR test became reactive after serial dilution, supporting a possible prozone phenomenon. Histopathological examination demonstrated psoriasiform features, which, although not specific, were supportive in the appropriate clinical context. The presence of dermal plasma cell infiltration, together with spongiosis and vacuolar degeneration of the basal layer, and without Munro microabscesses is suggestive of secondary syphilis.

HIV treatment was given TLD regimen and cotrimoxazole 960 mg once a day. The patient was treated for syphilis with benzathine penicillin G at a dose of 2.4 million units administered once weekly for three consecutive weeks intramuscular injection. The patient reported no history of penicillin allergy. This was further confirmed by an intradermal allergic test dose of 0.1 mL, which elicited no allergic reaction. Each weekly dose consisted of intramuscular injections of 1.2 million units of benzathine penicillin G into each gluteal region. The patient was observed for 30 minutes after each injection. The treatment course was completed uneventfully, and there was no Jarisch-Herxheimer reaction.

The patient was advised to undergo repeat RPR titer testing on 1, 3, 6, 12, 18, and 24 month after last injection, in accordance with WHO recommendations, to evaluate treatment response. The patient's clinical symptoms have resolved and the serologic syphilis test was decline **(Table 1)**, according to outpatient follow-up.

Table 1 Follow up titer result.

	Month- 0	*Month-0 after dilution*	*Month-1*	*Month-3*
TPHA titer	1/2560	1/2560	1/2560	1/650
RPR titer	Non-reactive	1:32	1:16	1:4

Discussion

Syphilis continues to represent a substantial public health concern among marginalized populations in Indonesia, particularly among men who have sex with men (MSM).[6] There are more reports of atypical forms of syphilis. The most variety of lesions is seen in the secondary stage.[4] The most prevalent clinical sign of secondary syphilis is cutaneous manifestation. The phrase "great imitator" refers to the wide range of clinical presentations. Macular or maculopapular erythematous rash that appears on the torso and extremities is the most common clinical manifestation. Rarely, a lesion with a thicker scale may resemble psoriasis (psoriasiform), as was the case in this instance.[3] Psoriasiform syphilis is one of the unusual types that mimics psoriasis, the most common inflammatory illness. The presence of lesions on the palms and soles is a strong indication of syphilis.[4]

Syphilis can be diagnosed through serological testing, although serological test results can vary in most HIV-infected syphilis patients. If syphilis is clinically suspected, but the serological test is nonreactive, or the interpretation is unclear, other methods may be necessary to confirm the diagnosis. Direct detection of *T. pallidum* such as darkfield microscopy, direct fluorescent antibody test, molecular test (PCR) and also histopathologic examination not essential for a diagnosis of syphilis.[4,7] In this case, the histopathological examination revealed several plasma cells and perivascular lymphocytes are visible in the dermis which is pathognomonic sign of secondary syphilis.

A misleading negative reaction brought on by excessive antibody titers is known as the "prozone phenomenon". The prozone effect is more common in secondary syphilis, syphilis with co-infection with HIV, and pregnancy. According to reports, the prozone phenomenon occurs between 0.5% and 2% of the entire time.[8] Pregnancy, the stage of syphilis, co-infection with HIV, and neurosyphilis are all related with the prozone phenomenon. Patients with syphilis are at increased risk of acquiring HIV, and conversely, individuals with HIV are more susceptible to syphilis. In cases of syphilis and HIV co-infection, abnormal B-cell function and exaggerated responses to antigenic stimulation may lead to excessive antibody production. Furthermore, because the primary syphilitic chancre is typically painless and transient, syphilis in MSM is more likely to remain clinically unrecognized, thereby increasing vulnerability to HIV transmission. HIV-induced B-cell dysfunction has also been associated with a higher incidence of the prozone phenomenon, which may result in false-negative serologic findings and consequently delay or obscure the diagnosis and treatment of syphilis.[8] In this case initially the result of RPR was nonreactive response which occurs because of overwhelming antibody titers, after dilution the RPR became reactive 1:32.

In patients with atypical cutaneous manifestations, including psoriasiform secondary syphilis, the prozone phenomenon may delay diagnosis and treatment. Therefore, when clinical suspicion remains high despite a nonreactive nontreponemal test, repeat testing with serial serum dilutions is strongly recommended to reveal true seroreactivity and ensure timely diagnosis.[5,8]

Conclusion

Clinicians should maintain a suspicion for psoriasiform secondary syphilis in patients with HIV presenting with atypical cutaneous manifestations. False-negative serology may occur due to the prozone phenomenon or seronegative syphilis; therefore, repeat diluted testing and clinicopathologic correlation are essential for timely diagnosis and treatment.

Acknowledgement

We gratefully thank Faculty of Medicine Univeristas Airlangga, Surabaya, Indonesia for supporting this study.

Declaration of patient consent Authors certify that they had obtained all appropriate patient's consent.

Financial support and sponsorship None.

Conflict of interest No conflict of interest.

Author's contribution

IF, FS: Identification and management of the, manuscript writing.

ANH, DM, SW, A, RIA: Identification and management of the case, critical review of the manuscript before publishing.

All authors have given final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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