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Case Report

Papular pruritic eruption as a clinical indicator of an undiagnosed AIDS patient: A case report

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Abstract Cutaneous disorders are one of the most common complications of patients with Human Immunodeficiency Virus (HIV) infections and acquired immunodeficiency syndrome (AIDS). The clinical manifestation of these cutaneous disorders' ranges from infections, malignancies, and other inflammatory conditions that can be distinguished based on the severity of infection through assessment of the number of CD4 lymphocyte cells. The misdiagnosis rate of these cutaneous disorders is high, particularly in patients with unclear HIV status or undiagnosed HIV infections. Papular pruritic eruption (PPE) is one of the cutaneous manifestations of HIV that occur mostly in patients with a low count of lymphocyte CD4 cells (<200 cells/uL). We report a case of a 49-year-old male patient with PPE that was initially diagnosed with prurigo nodularis with no improvement after topical potent corticosteroid treatment. A more thorough history taking, physical examination, and confirmation through histopathology examination revealed that the patient was an undiagnosed AIDS patient with a total lymphocyte CD4 cell count of 45 cells/uL with PPE. The patient was successfully treated using a combination of antiretroviral (ARV), oral antihistamines, and topical corticosteroids with significant clinical improvements, prompting physicians to be more aware of the possibility of PPE when faced with unspecific dermatitis/ prurigo-like clinical manifestation with no improvement after conventional corticosteroid treatment.

Key words
Papular pruritic eruption; HIV; AIDS; undiagnosed.

Introduction

According to data from the World Health Organization (WHO), it is estimated in 2021 there are 38.4 million people living with HIV globally.[1] Furthrmore, "Report on the Development of HIV/AIDS and Sexually Transmitted Diseases" published by the Indonesian Ministry of Health in the first quarter of 2021 also reported an uptrend in the number of confirmed HIV cases from year to year. Cumulatively, the number of confirmed HIV patients in Indonesia until March 2021 was 427,201 cases or around 78.7% of the estimated 543,100 people with HIV/AIDS (PLHIV).[2]

Based on the epidemiological data above, it can be concluded that there are approximately 115,899 undiagnosed PLHIV cases. The age group most affected is between the ages of 25-49 years (70.7%), dominated by males (62%) compared to females (38%) with a ratio of 5:3. Furthermore, of the total number of PLHIV in Indonesia, only 269,289 or approximately 63% are undergoing antiretroviral (ARV) treatment.[2]

Cutaneus manifestations in HIV patients, especially untreated ones are generally higher and more severe compared to patients undergoing ARV treatment. These various

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Figure 1 Multiple erythematous papules on the bilateral upper extremities along with multiple erythematous papules and nodules on the bilateral lower extremities.

clinical manifestations include infection, malignancy, and drug reactions. In addition, the presence of skin disorders in HIV patients can also aid in the diagnosis of an HIV infection itself.[3,4]

Papular pruritic eruption (PPE) is one of the most common cutaneous manifestations in HIV patients, with a prevalence rate varying between 11-46%. The condition is more prominent especially in patients located in the tropical or subtropical areas. Clinical symptoms of PPE are characterized with symmetrical papular pruritic eruptions, more prominantely on the chest and extremities, with usual sparring of the mucosal membranes, palms and feet. PPE has a high morbidity rate and can significantly affect the quality of life of HIV patients.[5]

We report a case of a 49-year-old male patient with multiple symmetrical pruritic erythematous papules and nodules on the upper and lower extremities initially diagnosed with prurigo nodularis with an undiagnosed HIV infection. The patient exhibited a low CD4 lymphocyte cell count (45 cells/uL) with histopathological findings suggestive of PPE. Clinical improvement were found after the patient undergone routine ARV treatment for 4 months combined with oral antihistamines along with topical corticosteroids and emollients.

Case report

A 49-year-old male patient visited the outpatient clinic with complaints of erythematous rash on both arms and legs 3 months prior. Lesions initially started as a few erythematous rash on the legs that later spread to both arms. Severe pruritus was also experienced that hindered the patient's daily activities and sleep. The patient said he was diagnosed with prurigo nodularis and was using corticosteroid creams in the past two months with limited improvement and recurrences.

Physical examination found the patient was slightly lethargic, with normal vital signs. Dermatological examination found multiple erythematous papules on the bilateral extremities along with erythematous papules and nodules on the lower extremities more prominently on the posterior left femoral and right gastrocnemius (**Figure 1A-D**).

A more thorough history taking revealed that the patient experienced malaise and recurring fevers, lost of appetite, along with a significant weight loss of 15kg in the past 6 months. The patient works as a police officer and admitted to a history of unprotected sexual intercourse with a sex worker and gonorrhea around 20 years prior. The patient also had a history of multiple

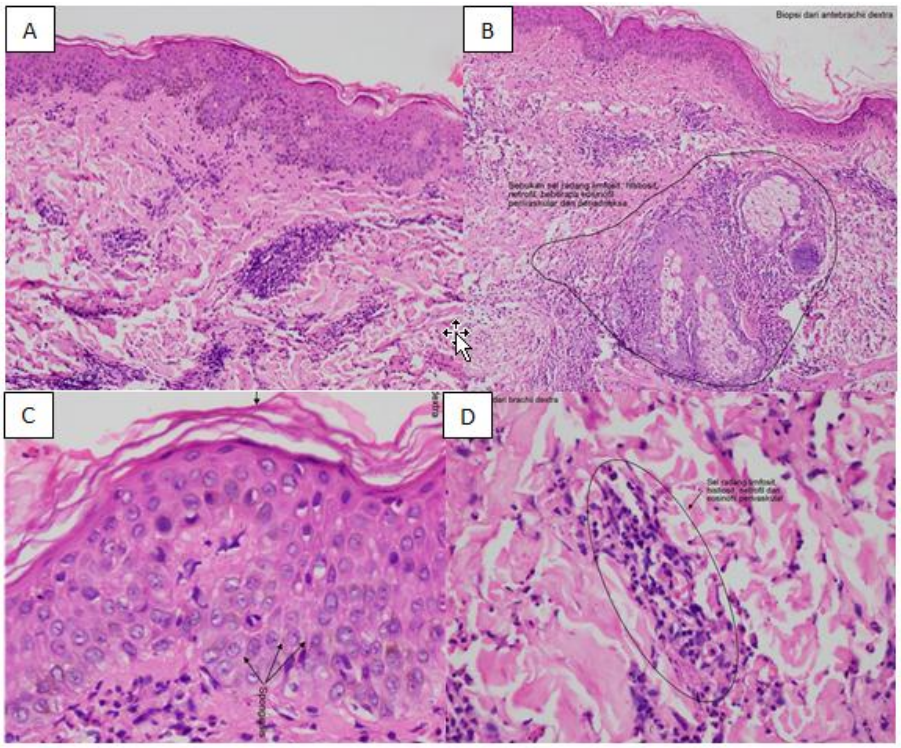

Figure 2 Epidermal Hyperkeratosis (A/100x & C / 400x); Lymphocytes, Neutrophils and Eosinophils on the Dermis along with Perivascular and Periadnexal Eosinophils (B / 100x & D / 400x)

hospitalization in the past 2 years with pneumonia.

Routine blood examination found leucopenia (2,032/uL) and positive anti-HIV immunosereology test. A follow-up molecular examination of HIV-1-RNA wasalso positive with a viral load of 9.31x10^5 copies/ml and 5.97 log *copies*/ml respectively. A low CD4 lymphocyte cell count was observed (45 cells/uL) along with a low CD4% (4.1%). The CD4:CD8 ratio of the patient was (0.07).

Histopathological Examination through punch biopsy from one of the papules found psoriasiform epidermal hyperplasia, spongiosis, and hyperkeratosis. Inflammatory cells of lymphocytes, histiocytes, neutrophils were found on the dermis, along with perivascular and periadnexal eosinophils (**Figure 2A-D)**.

Based on these findings, the patient was diagnosed with AIDS and PPE. A combincation treatment using oral antihistamines of cetirizine 10mg daily, moisturizers, and potent topical corticosteroids of desoximehtasone cream applied twice daily was given. In addition the patient was also started with a daily combined dose of ARV consisting of 50mg dolutegravir sodium, 300mg lamivudine, and 300mg tenofovir disoproxil fumarate. The patient was also advised to check the HIV status of his wife and children as well as the possible side effects of ARV treatment. A four-month follow-up after ARV treatment found significant clinical improvements on the cutaneous lesions, leaving only minimal number of erythematous papules and multiple post- inflammatory hyperpigmentation (**Figure 3A-D**).

A follow-up laboratory examination found increased leukocytes (4,200/uL), CD4 lymphocyte cell count (198 cells/uL), CD4% (8.9%), and CD4: CD8 ratio (0.21).

Figure 3 Significant clinical improvements after four months of treatment.

A decrease of HIV-1-RNA viral load (1.54x10^2 copies/ml and 2.19 log copies/ml respectively) was also noted. The patient was scheduled for regular check-ups every 6 months.

Discussion

Immunosuppression due to HIV infection can cause a wide array of clinical manifestations including the skin. In addition, clinical symptoms tend to be more severe in undiagnosed and untreated patients due to the depletion of CD4 lymphocyte cells and the overall immune system.[6,7] It is estimated that cutaneous manifestation affect 90% of untreated PHLIV.[1]

PPE is one form of cutaneous manifestation in HIV patients, which is attributed to immunological changes mainly associated with the patient's CD4 cell count. The condition is more prominent in AIDS patients with a low CD4 cell count (<200 cells/uL) or CD4% <14%, and a higher viral load compared to other HIV patients.[6] The etiology of PPE is still unknown. One hypothesis suspects that PPE is an immunological response caused by the shifting of Th1 to Th2 cells accompanied with an increase in IL-4 and IL-5 production resulting in eosinophilia.[8] More recent studies suggest that PPE is a cutaneous manifestation as a result of a hypersensitivity reaction to certain antigens from insect bites in HIV patients.[6]

PPE is characterized with the onset of generalized papular eruptions especially on the trunks and extremities. Upon physical examination, discrete erythematous papules and nodules can be observed with diffuse distribution such as in this case, where the majority of lesions were found on the lower extremities.[9,10]

The diagnosis of PPE can usually be made clinically based on history taking and physical examination. Confirmation of the patient's HIV status through serological tests such as positive anti-HIV along with a sharp decrease in CD4 lymphocyte cells can also aid in diagnosis. More invasive examinations such as histopathology are not routinely performed but can aid in distinguishing PPE from other HIV related dermatosis such as eosinophilic folliculitis (EF). In EF lesions, similar manifestation such as pruritic papules and follicular pustules can be found, mostly on the seborrheic areas. In our case, histpathological features confirmed the diagnosis of PPE with spongiosis, and infiltration of perivascular lymphocytes, as well as eosinophils found on the upper dermis were observed. Conversely, in patients with EF, histopathological examination is usually

dominated with infiltration of eosinophils, lymphocytes, and histiocytes in the follicles.[9] Other differential diagnoses that can be considered in our case include insect bites, scabies, drug eruptions, and papulonecrotic tuberculosis.[6]

One of the possible causes for misdiagnosis of prurigo nodularis in this patient, was due to the previous unestablished HIV status. Patients with undiagnosed HIV can be challenging. This caused a delay in the initiation of ARV treatment leading to evolution into AIDS which will increase the morbidity and mortality rate of HIV patients. In addition, undiagnosed HIV patient may also increase the risk of HIV spread, where in this case transmission to the patient's wife and two children were noted.[11]

The recommended first-line ARV treatment in adult patients with HIV is highly active antiretroviral therapy (HAART) using a combination of several types of simultaneously consisting of two types of nucleoside reverse-transcriptase inhibitors (NRTIs) plus one type of non-nucleoside reverse-transcriptase inhibitor (NNRTI) or one integrase inhibitor (INSTI). Based on the WHO guideline, the recommended first-line combinations are tenofovir, lamivudine/ emtricitabine and efavirenz. However, if conditions where this combinations is unavailable, several alternative combinations can be selected, such dolutegravir, lamivudine and tenofovir in our case.[12-14]

With routine ARV treatment for 4 months, out patient exhibited significant clinical improvements. While remission of symptoms can be achieved through ARV treatment, it may take quite a long time for some patients after the initiation of the ARV to experience improvements. One study by WHO reported that 37 out of 43 patients or 83% of PPE patients experienced resolution within 6 months of ARV treatment.[5] In addition, the use of symptomatic treatments such as oral antihistamines and topical corticosteroids can also help relieve symptoms.[8] Post-inflammatory hyper-pigmentation and excoriation are common findings in treated PPE patients Such as in our case where we found multiple hyperpigmented macules and minimal erythematous papules upon a four-month follow-up.[5]

The initiation of ARV however, in some cases may lead to other cutaneous disorders that need to be addressed to the patient prior to treatment. Most notably the possibility of exacerbation of other cutaneous abnormalities due to the improvement of the immune system/ immune reconstitution inflammatory syndrome (IRIS).[5,6]

In severe cases of PPE that does not improve with AR, the use of narrowband-ultraviolet B (NB-UVB) may be considered as reported in a paper by Bellavista, *et al*. who reported the successful use of NB-UVB in persistent PPE within 7 weeks that achieved full remission of papules and pruritus in a PPE patient who had already experienced an increase in CD4 after ARV treatment for 3 months. The initial dose of NB-UVB was 0.4J/cm^2 with an incremental dosage increase of 0.1J/cm^2 on each visit with dosage up to 0.9J/cm2. The cumulative dose received was 12.9J/cm^2.[8]

After improvement of lesions, the patient was then advised to do periodic serological examination. The recommendation by WHO regarding the follow-up of viral load are 6 months and 12 months after the initiation of ARV treatment, followed with periodic examinations with a 12-month interval. While examination of CD4 lymphocyte cell count, should be performed every 6 months.[12]

Conclusion

PPE is a cutaneous manifestation that often

occur in AIDS patients with a low CD4 cell count of <200 cells/uL. The rate of misdiagnosis is high, especially in undiagnosed HIV patients, Increased awareness should be performed by physicians when encountering chronic pruritic dermatosis that does not resolve using conventional treatments.

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