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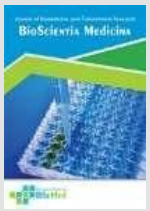

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Psychological Stress Induced Recurrent Genital Herpes: A Case Report

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A B S T R A C T

Background: Herpes simplex virus type 2 (HSV-2) infection can be caused by genital herpes with a high recurrence rate. Recurrent genital herpes affected patients' quality of life. Precise management is needed to prevent the progression of the disease. **Case presentation:** This study reported a 34 years old male with recurrent genital herpes. The patient developed painful vesicles in the genital area, which turned into an ulcer. History of genital herpes and gonorrhoea urethritis were reported and had been treated. The patient had a history of having unprotected sexual intercourse with multiple partners and reported having psychological stress within 1 month. DLQI score was 12, and the DASS score was 5-85, which confirmed that the patient had anxiety. Vesicles and erosion were found in the genital area. Tzanck test showed multinucleated giant cells with borderline anti-HSV-2 IgG serologies in 2 occasional evaluations. Acyclovir 3x400 mg for 5 days was used as therapy, and no lesion was found at follow-up. **Conclusion:** Psychological stress was found to be a risk factor for recurrent genital herpes

1. Introduction

Genital herpes is a sexually transmitted disease (STI) caused by herpes simplex virus type 2 (HSV-2). Infection of HSV-2 manifests as painful confluence vesicles, which can develop into ulcers.[1] It is estimated that there are 187 million patients between 15-49 years old who have genital ulcers caused by HSV. Moreover, as much as 95% of them were infected by HSV-2. However, the incidence of HSV-2 infection in South East Asia is 3,5% for females and 2,6% for the male population.[2]

The HSV-2 causes a long-life infection which is divided into the primer infection phase followed by a latent period and a reactivation period. The presence of HSV-2 can invade epithelial cells and the periaxonal sheath of sensory neurons to nervous ganglions. Risk factors such as stress, fever, microbes infections, UV radiations, hormonal imbalance, or other immunosuppression conditions may cause reactivation similar to primary infection manifestation.[3,4] Previous studies have reported psychological stress can be the only risk factor for recurrent intraoral herpes caused by HSV-1 and also affect the treatment progression.[5] There was no previous study that reported psychological stress as a risk factor for recurrent genital herpes.

Recurrence of genital herpes can decrease patients' quality of life. Sexual intercourses, occupations, and social well-being can be affected. Pharmacological and psychosocial interventions are needed to treat recurrent genital herpes.[6] It has been recommended that the recurrence of genital herpes more than 6

times in a year need to be treated with a higher dose of antivirals.[7] Therefore, an evaluation of the risk factors, including psychological stress, that cause recurrent genital herpes is needed to prevent further progression.

2. Case Presentation

A 34 years old man was admitted to the dermatology and venereology outpatient department of Dr. M. Djamil General Hospital Padang on April 20th, 2022, with a chief complaint of having painful vesicles at the penile shaft since 3 days ago. Two days before the eruption, the patient had arthralgia and muscle soreness, but no fever or headache was reported. One day prior to admission, the vesicles were broken and turned into excoriation wounds. There was a history of psychological stress, sleep disturbance, anxiety, and uncomfort feeling upon micturition within 1 month. Vesicles at other parts of the body, self-limiting genital ulcers, topical medicine or herbs, trauma, warts, rash, weight loss, mouth ulcers, night sweats, tattoos, transfusion, drugs, and hair loss were denied.

The patient had been married with 2 children. He actively had genito-genital sexual intercourse without a condom with his wife. His wife had no genital complaints. He had his first sexual intercourse with a woman in 2010 and had multiple sexual partners. He did only genito-genital sexual intercourse without a condom with women. In the last 6 months prior to admission, the patient started to have unprotected genito-genital sexual intercourse with commercial sex workers.

The patient had a history of purulent urine 4 months ago and was treated with ciprofloxacin 2x500 mg for 5 days and a single injection at his buttocks by a dermato-venereologist in another city. There was a history of genital herpes 1,5 months prior to admission, which was treated with acyclovir 5x200 mg for 7 days. One month prior to admission, the patient was diagnosed with gonorrhoea urethritis and treated with cefixime 400 mg single dose. No other risk factor was found.

Penile physical examination revealed millary confluent vesicles with edema, erosion, and erythema at 1/3 left side distal of the penile shaft. There was minimal secretion from the external urethral orifice after prostate massage. There was no palpable lymph node in the inguinal area. The assessment of dermatology life quality index (DLQI) score was 12 (great impact on patient's life), and the depression anxiety and stress scale (DASS) score was 5-8-5 (mild depression, moderate anxiety, and normal stress). These scores define that the patient had psychological alteration and his quality of life had been impacted.

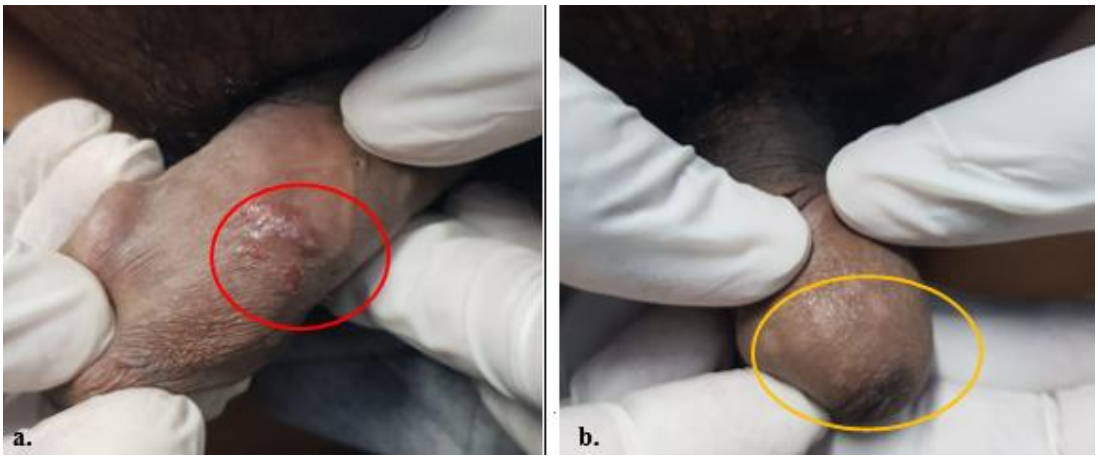

Figure 1. Penile examination on April 14th, 2022. (a) Confluence vesicles with erosion at 1/3 distal of the penile shaft (red circle). (b) Hypopigmented macules from previous genital herpes lesion (yellow circle).

Tzanck test from the base of the lesion revealed multinucleated giant cells. Negative-gram stained coccus bacteria with 30-40 polymorphonuclear (PMN) cells were found from erosion. No bacteria was found from gram-stain or Thayer Martin culture of orifice secretion. Serology for Anti-HSV-2 Immunoglobulin M (IgM) was evaluated on April 20th and May 13th with borderline results. evaluation of venereal disease research laboratory (VDRL), treponema pallidum hemagglutination assay (TPHA), and human immunodeficiency virus (HIV) were non-reactive. These findings define that the patient had no immunocompromised disease.

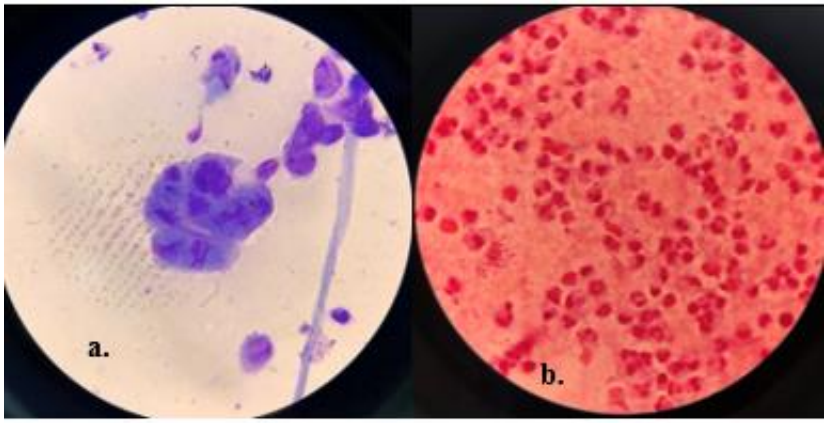

Figure 2. Laboratory evaluation. (a) Tzanck test revealed multinucleated giant cells. (b) Negative-gram stained coccus bacteria with PMN.

The patient was diagnosed with recurrent genital herpes and treated with acyclovir 3x400 mg for 5 days. Sexual abstinence was advised until the treatment was completed, and he asked his wife to have a screening. A follow-up examination on May 13th, 2022, revealed no genital lesion and the patient had no complaints.

Figure 3. Follow-up evaluation on May 13th, 2022.

3. Discussion

This study has reported a 34 years-old man with recurrent genital herpes. The patient complained of having painful vesicles at the penile shaft in the last 3 days with a history of arthralgia and muscle soreness. Vesicles turned into excoriation wounds 1 day before admission. There was a history of psychological stress and sleep disturbance. The patient had unprotected genito-genital sexual intercourse with multiple partners. There was a history of genital herpes,

gonorrhoea urethritis, and purulent urine at 1,5, 1, and 4 months before admission and had been treated. Physical examination showed confluent vesicles with erosion, edema, and erythema at 1/3 distal penile shaft. Tzanck test revealed multinucleated giant cells. Anti-HSV-2 IgM serology was evaluated twice, with both being borderline. The patient was diagnosed with recurrent genital herpes and treated with acyclovir 3x400 mg for 5 days. No lesions and complaints at follow-up examination.

Looker et al. (2020) showed that the prevalence of HSV-2 infection among South East Asia women with genital ulcers was higher compared to men. Moreover, HSV infection was found to be more frequent in older patients, with the peak at 45-49 years old.[2] Patel et al. (2012) stated that HSV infection was higher in men but mostly asymptomatic.[8]

Genital herpes is a STI caused by HSV-2 in sexual intercourse with a previously infected genital partner. Wang et al. (2012) revealed HSV-2 infection among commercial sex workers was 58,3%, with the highest risk being those who had worked more than 3 months.[9] Margaret et al. (2015) found that 28,5 HSV-2 was transmitted from men to women during 1.000 unprotected sexual intercourse. On the other hand, transmission of HSV-2 from women to men was 1,7 cases among 1.000 unprotected sexual intercourse. A condom can reduce as much as 65-96% of transmission.[10] Our patient had a history of unprotected multiple-partner sexual intercourse with commercial sex workers as a risk factor for acquiring HSV-2 infection. However, there is no study that reported unprotected sexual intercourse as a risk factor for recurrent genital herpes. Therefore, we rule out the patient's history of sexual activity as a risk factor for recurrent genital herpes.

The sexually transmitted disease was found to be correlated with HSV infection. Kenyon et al. (2016) described that there was a significant correlation between syphilis and HSV-2 infections.[11] Moreover, a meta-analysis from Esber et al. (2015) found that bacterial vaginosis patients had a 1,55 times higher risk of having HSV-2 infection.[12] However, there was no study that observed the correlation between gonorrhoea urethritis with HSV-2 infection. Therefore, we had not concluded that our patient's history of gonorrhoea urethritis was a risk factor.

The patient was evaluated for the DLQI score, which was 12 (had a great impact on the patient's quality of life), and the DASS score was 5-8-5 (mild depression, moderate anxiety, normal stress). Suryawati et al. (2021) concluded that DLQI correlated to psychological stress.[13] Suniti et al. (2018) reported a case of recurrent intra-oral herpes caused by HSV-1 infection with psychological stress as a risk factor. The patient was previously treated for 3 months without any good progression. However, after psychological treatment, the lesions were cured.[5] Therefore, psychological stress in patients was suspected to be the only risk factor for recurrent genital herpes.

Recurrence of genital herpes is caused by activation of HSV-2, which previously had been in the shedding period. Disruption of a cluster of differentiation (CD)-8 cells can cause HSV-2 ability to undergo replication. Maydych et al. (2017) found that the population with psychological stress had a decrement in the number and function of CD8 cells.[14] Sungkono et al. (2020) observed that DASS score was correlated with cortisol level.[15] Patterson et al. (2013) found that cortisol levels had a significant negative correlation with CD8 cells.[16] Ives et al. (2017) tried to explain the correlation between glucocorticoid and HSV reactivation. It was found that the IB4+ type of neuron had a greater number of glucocorticoid receptors in the HSV-2-infected neuron model. Treatment with glucocorticoid was found to increase proliferation, determined by DNA load, of HSV-2 in previously infected neurons.[17]

The Tzanck test is a rapid and cost-effective cytodiagnostic evaluation for viral infection among skin lesions. Cases caused by viral infection were described to have multinucleated giant cells. Banihashemi et al. (2014) compared Tzanck test to viral cell culture as a gold standard with the result that sensitivity and specificity for HSV were 90% and

100%.[18] However, Chaiyabutr et al. (2021) revealed that Tzanck test had a better sensitivity and specificity for varicella zoster virus detection rather than HSV.[19] Serology evaluation for HSV-2 can be done with both immune-fluorescence or ELISA. LeGoff et al. (2014) found that the ELISA method detected serum antibodies and had a sensitivity of 93-98% and specificity of 93-99%. This can help to differentiate HSV-1 and HSV-2 but was not recommended to be used for general population screening. Serology evaluation for recurrent genital herpes can show a positive result for IgG HSV-2.[20]

World Health Organization (2016) recommended acyclovir over valacyclovir and famciclovir as HSV infection treatment. Acyclovir can be given 400 mg three times a day for 5 days, 800 mg twice a day for 5 days, or 800 mg three times a day for 2 days. Acyclovir was chosen due to its ability to decrease viral shedding duration and give a shorter duration for resolution, 1,32 and 1 day.[7] A randomized-controlled trial by Johnsotn et al. (2012) found there was no difference between acyclovir and valacyclovir for recurrent rate.[21] Our patient was treated with acyclovir 400 mg three times a day for 5 days and showed full recovery at the follow-up evaluation.

Our study reported a case of recurrent genital herpes with psychological stress predicted to be the only risk factor for recurrence. However, further evaluation is needed to confirm the pathophysiology and correlation between them. Moreover, we had not re-assessed DLQI and DASS scores at the end of treatment, which may provide information that confirms our therapy can reduce psychological stress. Cortisol level examination can give stronger evidence for the determination of psychological stress as a risk factor for recurrent genital herpes in a patient who was not found to have other risk factors.

4. Conclusion

This study reported a patient with psychological stress as the only risk factor for developing a recurrency of genital herpes

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