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 confluent vesicles, which can develop into ulcers. 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.

The HSV-2 causes a long-life infection which is divided into the primer infection phase followed by a latent period and 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.

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.

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 and headache were 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 discomfort 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
sweat, tattoo, 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 gonorrhea urethritis and treated
with cefixime 400 mg single dose.

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 secretions from the external urethral orifice after
prostate massage. There was no palpable lymph node
in the inguinal area. Assessment of Dermatology Life
Quality Index (DLQI) score was 12 (great impact on
patient’s life), and Depression Anxiety and Stress Scale
(DASS) score were 5-8-5 (mild depression, moderate
anxiety, and normal stress).

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
secretions. 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.
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.

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 lesion 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 among 45-49 years old.2 Patel et al. (2012) stated that HSV infection was higher in men but mostly asymptomatic.6 Our report found a case from 34 years old man, which is different from the most frequent population stated by previous studies.

Genital herpes is a STI caused by HSV-2 among sexual intercourse with a previously infected genital partner. Kenyon et al. (2013) found that the increase in HSV-2 infection prevalence was associated with the increase in sexual activity.7 Beydon et al. (2011) show that sexual activity before 13 years old had 7.3 times higher risk of being infected by HSV-2.7 Wang et al. (2012) revealed HSV-2 infection among commercial sex workers was 58.3% with the highest risk were those who had worked more than 3 months.8 Margaret et al. (2015) found that 28.5 HSV-2 transmitted from men to women among 1.000 unprotected sexual intercourses. On the other hand, the 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% transmission.9 Our patient had a history of unprotected multiple partner sexual intercourse with commercial sex workers as a risk factor for acquiring HSV-2 infection.

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.10 A randomized-controlled trial by Stachan et al. (2011) found that daily stress, anxiety, and depression hand associated with the recurrence of genital herpes. An external stressor can cause a 10% higher frequency of lesions. The most rapid symptom can present 5 days after psychological stress. However, there was no study that confirmed the direct mechanism for stress to reactivate HSV-2.11 Maydych et al. (2017) found that the population with psychological stress had a decrement of the number and function of CD8 cells.12 Patients were evaluated for DLQI score, which was 12 (had a great impact on patient’s quality of life), and DASS score was 5-8-5 (mild depression, moderate anxiety, normal stress). Therefore, psychological stress in the patient was suspected to be the 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.13 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.14 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.

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 the tzanck test to viral cell culture as a gold standard, with the result sensitivity and specificity for HSV being 90% and 100%.15 However, Chaiyabutr et al. (2021) revealed that the tzanck test had a better sensitivity and specificity for varicella zoster virus detection rather than HSV.16 We conducted an additional laboratory evaluation for a viral agent after finding the patient’s tzanck test revealed multinucleated giant cells.

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-2.17

Shameen et al. (2011) had evaluated the accuracy of antibody serology of HSV-2 with PCR or cell culture as gold standards. Sensitivity and specificity for serology evaluation compared to culture were 100% and 59%.18 Gupta et al. (2018) found that there was no recurrent genital herpes patient who had positive Anti-HSV-2 IgM, and only 38.9% of patients had positive Anti-
HSV-2 IgG. Moreover, 55.6% of patients had negative serology for Anti-HSV-2 IgM and IgG. The diagnosis of reactivation was made if there were 2 evaluations with 2 weeks apart revealed a significant increase of IgG titers.\textsuperscript{19} Our patients had borderline Anti-HSV-2 IgM serology among 2 evaluations more than 2 weeks apart. This can be caused by therapy before the second evaluation. Confirmation evaluation with PCR or cell culture may be needed for patients who are suspected of recurrent genital herpes with negative serology evaluations.

World Health Organization (2016) had 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.\textsuperscript{20} A randomized-controlled trial from Johnston et al. (2012) found there was no difference between acyclovir and valacyclovir for recurrent rate.\textsuperscript{21} Our patient has treated with acyclovir 400 mg three times a day for 5 days and showed full recovery at follow-up evaluation.

4. Conclusion

This study reported recurrent genital herpes from 34 years old man with unprotected multiple partner genito-genital sexual intercourses. Psychological stress was suspected to be the main risk factor for recurrent genital herpes. Acyclovir 400 mg three times a day for 5 days was effective in treating recurrent genital herpes.

5. References

19. Gupta A, Malhotra S, Oberoi L, Kaur T, Malhotra SK, et al. Section: Microbiology seroprevalence of HSV-2 in STI clinic attendees and non high risk controls in a tertiary care hospital in North India Section: