

# Recurrent vulvovaginal candidiasis in a patient with systemic lupus erythematosus: A case report

AM Evanti, E Nurfaiqoh, AW Pramudita, EY Ellistasari

Departement of Dermatology and Venereology, Faculty of Medicine, Sebelas Maret University, Dr. Moewardi General Regional Hospital, Surakarta, Indonesia.

**Abstract** A 30-years-old woman complaint of intermittent itchy yellowish vaginal discharge since 1 year ago. The patient has SLE since 6 years ago. Inspeculo examination showed vaginal and cervical erythema accompanied by yellowish white, cheese-like discharge. Direct microscopic examination using 10% KOH showed budding yeast cells and pseudohyphae. Culture examination showed *C. glabrata* and resistance to fluconazole. The patient was treated with intravaginal nystatin 100.000 iu for 14 days followed by 100.000 iu for 14 days every month. Clinical improvement was found in two months after treatment.

**Key words**

Fluconazole; Recurrent vulvovaginal candidiasis; Systemic lupus erythematosus.

## Introduction

Recurrent vulvovaginal candidiasis (RVVC) is an infection of the vulva and vagina caused by *Candida* species with at least four attacks in the last 12 months.<sup>1</sup> *Candida albicans* is the fungus that most often causes RVVC, which is around 85-90% of all cases, with the remaining namely *C. glabrata*, *C. krusei*, *C. famata* and *C. tropicalis*.<sup>2</sup>

The clinical manifestation of vulvovaginal candidiasis are characterized by abnormal white, thick, cheese-like vaginal discharge accompanied by erythema, excoriation and pruritus on the vulva and vagina.<sup>2</sup> Culture examination is needed to determine *Candida* species, usually by using Sabourad dextrose agar.<sup>3</sup>

Patients with SLE have higher risk of RVVC where candida is an opportunistic microorganism that can cause infection in immunocompromised patient.<sup>4,5</sup> Immunosuppressant therapy such as corticosteroid and cyclosporine can also increase susceptibility to candida infection.<sup>6</sup>

Management therapy in cases of RVVC is the use of oral or intravaginal antifungal. Vulvovaginal infection caused by non-albicans candida usually does not respond well to fluconazole especially in *C. glabrata* infection which is quite difficult with high failure rate.<sup>7</sup> The use of nystatin 100.000 iu intravaginally at night for 12-14 days for at least 6 months is well tolerated and has a cure rate of 70-90% of cases.<sup>8</sup>

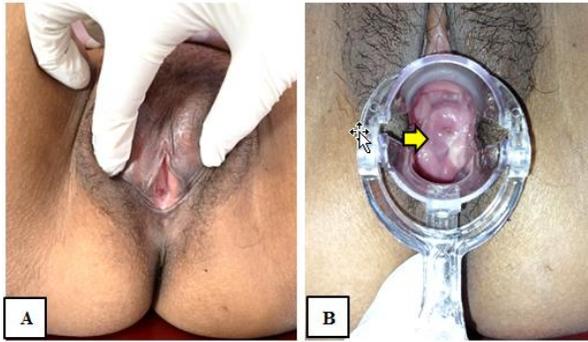
---

## Address for correspondence

Dr. Annisa Marsha Evanti  
Departement of Dermatology and Venereology,  
Faculty of Medicine, Sebelas Maret University, Dr.  
Moewardi General Regional Hospital, Surakarta,  
Indonesia.  
Email: annisamarshae@gmail.com

## Case Report

A 30-years-old woman came with chief complaint intermittent vaginal discharge for one year. She had vaginal discharge that turned



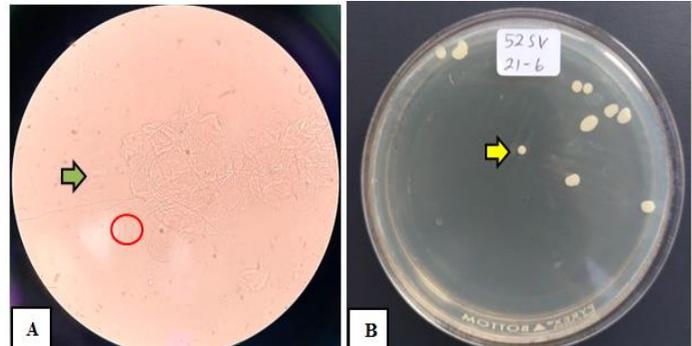
**Figure 1** (A) Labia major and minor showed no abnormalities (B) Cervical and vaginal regions are erythematous with white, lumpy, cheese-like discharge (yellow arrows).

milky yellow-white, lumpy, odorless and itchy. The discharge was increased, especially after sexual intercourse and did not affected by menstrual cycle. The patient also felt discomfort during sexual intercourse. She denied any fever and pain when urinating or defecating.

The patient had recurrent vaginal discharge >4 times since 1 year ago. She went to a dermatologist previously and was treated with metronidazole 500 mg and nystatin 100.000 Iu ovula for 7 days. She had a history of SLE since 6 years ago and was treated with cyclosporine capsules 50 mg twice daily, methylprednisolone tablets 4 mg twice daily and hydroxychloroquine tablets 200 mg daily. She used intrauterine device contraceptive but was removed 3 months ago. She changed her underwear 3-4 times daily and also vaginal douching.

External genitalia examination did not reveal any erythema, lumps, erosions or sticky discharge (**Figure 1A**). Inguinal lymph nodes revealed no enlargement. Internal genitalia revealed a cheese-like yellowish-white discharge, odorless and lumpy on the vaginal wall (**Figure 1B**). Her vaginal pH was 4 and amine test was negative.

Microscopic examination with 10% KOH showed the presence of pseudohyphae and



**Figure 2** (A) Microscopic examination with 10% KOH showed pseudohyphae (green arrows) and budding cells (red circles), (B) Culture examination with Saboroud dextrose agar showed *Candida glabrata* colonies (yellow arrows).

budding cells (**Figure 2A**). Vaginal swab culture showed colony of *Candida glabrata* that sensitive to voriconazole, micafungin, amphotericin B and flucytosine (**Figure 2B**). Based on history taking, physical examination and supporting examination, this patient was diagnosed with candidiasis vulvovaginalis caused by *Candida glabrata*.

Patient was treated with nystatin 100.000 Iu intravaginally for 14 days and repeated monthly for 6 months. Clinical improvement was seen in second month after the treatment. External genitalia examination did not reveal any erythema, erosions or secretions. Inspeculo examination showed no discharge and 10% KOH examination showed no pseudohyphae or budding cells.

## Discussion

Recurrent vulvovaginal candidiasis defined as at least four episodes of candida infection on vulva and vagina within 12 months with resolution of symptoms between episodes and positive microscopic or culture finding on at least two episodes when symptoms occurred. *Candida albicans* is the most common microorganism of RVVC in more than 85% cases followed by *Candida glabrata* with the incidence 4-5% of cases.<sup>9</sup>

Several factors have been associated with RVVC such as genetics (polymorphism, familial and ethnic), immune mechanisms (HIV infection, diabetes mellitus, pregnancy, aging, previous use of hormonal therapy, antibiotics, antifungals and/or immunosuppressants), low socioeconomic status and behaviors such as the use of contraceptives, sexual activity and vaginal douching.<sup>7,10</sup> In this case, the patient had been using intrauterine device (IUD) contraceptive and vaginal cleansing soap, which are risk factors for RVVC.

Patient with SLE are susceptible to several infection through two mechanisms, namely genetic factors and disease activity. The genetic factor is mannose-binding lectin (MBL), which is a receptor that activates the complement cascade through the lectin pathway. Individual with MBL allele variant have more active disease and a higher risk of infection. Susceptibility to infection is also affected by dysregulation of acquired immunity and severity of the disease. Lesion can damage skin and mucosal barriers that allow entry of microorganism.<sup>11</sup> Immunosuppressive therapy such as corticosteroid and cyclosporine can also increase susceptibility to candida infection. Corticosteroid can increase blood glucose levels which can alter the natural environment in vagina and promote the proliferation of candida. Corticosteroid can also impair the function of various microcirculation cellular components that associated with inflammatory response.<sup>6</sup> Cyclosporine selectively impairs T-cell function which increases the risk of infection.<sup>12</sup> A study by Selimoglu *et al.* in 2020 in Turkey reported fungal infections in 16.5% of liver transplant patients that use cyclosporine.<sup>13</sup> In this case, the patient had SLE that treated with methylprednisolone and cyclosporine for 6 years which can be risk factors for facilitating candida infection.

Zhang *et al.* in 2014 in China reported that 12.6% of *Candida* species isolated from patient with vulvovaginal candidiasis were resistant to fluconazole. Most of these fluconazole-resistant clinical isolates were identified as non-albicans *Candida* species such as *C. glabrata* and *C. krusei* (75%).<sup>14</sup> An important characteristic of non-albicans *Candida* species is intrinsic resistance or susceptibility to low-dose azole antifungals that result in treatment failure. Identification and antifungal resistance testing are necessary for optimal therapy, especially in cases where the diagnosis is made based on clinical manifestations and/or limited laboratory tests.<sup>7</sup> The emergence of drug resistance in *Candida* species is mainly due to mutations and overexpression of multidrug efflux pumps like ATP-Binding Cassettes (ABC). Overexpression of one of the ABC transporters, *Candida* Drug Resistance (CDR)-1, contributes to fungal cell resistance to azole derivatives include fluconazole, ketoconazole, itraconazole and miconazole but not nystatin and amphotericin B.<sup>15</sup>

Recurrent vulvovaginal candidiasis caused by non-albicans species can be treated using nystatin 100.000 I $\mu$  intravaginal for 14 days repeated every month for at least 6 months.<sup>8</sup> Nystatin is a broad spectrum Polyenes antifungal group that change the permeability of cell membranes by binding to ergosterol in the fungal cell wall and cause cell leakage and lysis.<sup>16</sup> Nystatin is fungistatic and fungicidal agent against wide variety of yeasts and yeast-like fungi.<sup>17</sup> Intravaginal nystatin has topical effect with low hepatotoxicity and no cross-reactions nor serious side effects have been reported.<sup>18</sup> Its use is contraindicated in patients with hypersensitivity to nystatin but it is safe in pregnancy and does not interfere fertility.<sup>19</sup> In this case, the patient was treated with nystatin 100.000 I $\mu$  intravaginally for 14 days every month for 6 months where clinical and microscopic

improvement was seen on 2 months after treatment showed by negative 10% KOH examination result.

### Conclusion

This case reports a 30-year-old woman with recurrent vulvovaginal candidiasis et causa *C. glabrata* and systemic lupus erythematosus. The diagnosis of RVVC was made based on a history of intermittent, itchy vaginal discharge for >4 episodes in the past year. Genitalia examination showed a thick cheese-like yellowish-white discharge (cottage cheese-like appearance). Culture examination on vaginal swab showed *C. glabrata* that resistant to fluconazole. The patient was treated with nystatin 100.000 I $\mu$  intravaginally for 14 days monthly for 6 months. Clinical improvement was found two months after the treatment.

### References

1. Sobel JD. Recurrent vulvovaginal candidiasis. *Am J Obstet Gynecol.* 2016; **214(1)**:2-21.
2. Blostein F, Levin-Sparenberg E, Wagner J, et al. Recurrent vulvovaginal candidiasis. *Ann Epidemiol.* 2017; **27(9)**:1-35.
3. Riel SJ, Lardenoije CMJG, Oudhuis GJ, et al. Treating (recurrent) vulvovaginal candidiasis with medical-grade honey-concepts and practical considerations. *J Fungi.* 2021; **7(664)**:1-18.
4. Akimoto-gunther L, Bonfim-mendonça PDS, Takahachi G. Factors to recurrent vulvovaginal candidiasis: Chronic stress and reduced antioxidant capacity. *PLoS One.* 2016; **11(7)**:1-14.
5. Farr A, Effendy I, Tirri B, et al. Guideline: Vulvovaginal candidosis. *Mycosis Diagnosis, Ther Prophyl Fungal Dis.* 2021; **64(6)**:1-20.
6. Farhan MA, Moharram AM, Salah T, et al. Types of yeasts that cause vulvovaginal candidiasis in chronic users of corticosteroids. *Med Mycol.* 2019; **57(6)**:1-7.
7. Makanjuola O, Bongomin F, Fayemiwo SA. An update on the roles of non-albicans candida species in vulvovaginitis. *J Fungi.* 2018; **4(4)**:1-17.
8. Saxon C, Edwards A, Rautemaa-Richardson R, et al. British association for sexual health and HIV national guideline for the management of vulvovaginal candidiasis. *Int J STD AIDS.* 2020; **31(12)**:1124-44.
9. Talaei Z, Sheikhabaei S, Ostadi V, et al. Recurrent vulvovaginal candidiasis: Could it be related to cell-mediated immunity defect in response to Candida antigen? *Int J Fertil Steril.* 2017; **11(3)**:134-41.
10. Yassin MT, Mostafa AA, Al-Askar AA, et al. In vitro antifungal resistance profile of Candida strains isolated from Saudi women suffering from vulvovaginitis. *Eur J Med Res.* 2020; **25(1)**:1-9.
11. Barber MRW, Clarke AE. Systemic lupus erythematosus and risk of infection. *Expert Rev Clin Immunol.* 2020; **16(5)**:1-13.
12. Malpica L, Moll S. Practical approach to monitoring and prevention of infectious complications associated with systemic corticosteroids, antimetabolites, cyclosporine and cyclophosphamide in nonmalignant hematologic diseases. *Hematol (United States).* 2020; **20(1)**:319-27.
13. Selimoğlu MA, Kaya S, Güngör Ş, et al. Infection risk after paediatric liver transplantation. *Turk J Pediatr.* 2020; **62(1)**:46-52.
14. Zhang JY, Liu JH, Liu F Di, et al. Vulvovaginal candidiasis: Species distribution, fluconazole resistance and drug efflux pump gene overexpression. *Mycoses.* 2014; **57(10)**:584-51.
15. Chew SY, Than LTL. Vulvovaginal candidosis: Contemporary challenges and the future of prophylactic and therapeutic approaches. *Mycoses.* 2016; **59(5)**:262-73.
16. Sedigheh Hosseini S, Joshaghani H, Shokohi T, et al. Antifungal activity of ZnO nanoparticles and nystatin and downregulation of SAP1-3 genes expression in fluconazole-resistant candida albicans isolates from vulvovaginal candidiasis. *Infect Drug Resist.* 2020; **13(2)**:385-94.
17. Jeyachandran Manohari P, Cs V, Ps M, Janakiraman K. Formulation and evaluation of nystatin vaginal tablet. *Pelagia Res Libr.* 2017; **8(1)**:1-10.
18. Khalandi H, Masoori L, Farahyar S, et al. Antifungal activity of capric acid, nystatin, and fluconazole and their in vitro interactions against candida isolates from

- neonatal oral thrush. *Assay Drug Dev Technol.* 2020;**18(4)**:195-201.
19. Fan S, Liu X, Wu C, *et al.* Vaginal nystatin versus oral fluconazole for the treatment for recurrent vulvovaginal candidiasis. *Mycopathologia.* 2015;**179(1-2)**:95-101.