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To cite this article: Damla Akdağ, Hüsnü Pullukçu, Tansu Yamazhan, Dilek Yeşim Metin, Oğuz Reşat Sipahi, Beyza Ener & Meltem Işıkgöz Taşbakan (2021) Anidulafungin treatment for fluconazole-resistant *Candida albicans* vaginitis with cross-resistance to azoles: a case report, Journal of Obstetrics and Gynaecology, 41:4, 665-666, DOI: [10.1080/01443615.2020.1732893](https://doi.org/10.1080/01443615.2020.1732893)

To link to this article: <https://doi.org/10.1080/01443615.2020.1732893>



Published online: 21 Apr 2020.



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CASE REPORT



## Anidulafungin treatment for fluconazole-resistant *Candida albicans* vaginitis with cross-resistance to azoles: a case report

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### Introduction

Almost 75% of women experience vulvovaginal *Candida* infection at least once during their lifetime and 90% of these infections are due to *Candida albicans* (Marchaim et al. 2012). Both diagnosis and treatment of recurrent vulvovaginal candidiasis are important problems for physicians and patients. The local and systemic use of azole derivatives, especially fluconazole, is very common in the treatment of vulvovaginal candidiasis (Donders et al. 2010). However, the resistance to antifungals increases due to their frequent use, similar to antibacterial resistance and there are cases unresponsive to these agents (Karabay et al. 2018). Herein, we present the treatment and follow-up of a patient with resistant recurrent vaginal candidiasis.

### Case report

A 37-year-old woman with no comorbidity used topical and oral antifungal/antibacterial medications (including itraconazole and fluconazole) in the treatment of recurrent vulvovaginitis, and was hospitalised due to continuous complaints. An intense, white coloured, odourless vaginal discharge was observed on vaginal examination. Urine and vaginal swab samples were taken for mycological and bacteriological culture. After 48 hours of incubation, *Candida* spp were yielded in mycological culture of clinical specimens. The species were identified by the Dalmau method, according to their morphological characteristics. Additionally, species-specific peptide and protein models were identified by VITEK MS (bioMérieux, France) method. Then, the infection agent was identified as *Candida albicans*. Metronidazole (500 mg q8h i.v.) and high dose fluconazole (600 mg q24h i.v.) were initiated empirically for the high probability of dose-dependent resistant *Candida* infection, but there was no clinical response. The *Candida albicans* was isolated in culture, but the response to systemic fluconazole treatment for one week was inadequate. An antifungal susceptibility test was performed by microdilution method according to the CLSI M27-

A3 guidelines (Clinical and Laboratory Standards Institute 2008) and the MIC values were reported respectively; fluconazole 4 µg/mL (SDD), itraconazole 1 µg/mL (R), posaconazole 0.06 µg/mL (WT), voriconazole 0.25 µg/mL (SDD), anidulafungin ≤0.015 µg/mL (S), amphotericin B 0.06 µg/mL (WT). For the resistance mechanism, point mutation in the *ERG11* gene and *MDR1* and *MDR2* from efflux pumps were investigated and only the G464S mutation was detected in the *ERG11* gene. The treatment was switched to anidulafungin. Clinical response was achieved in the patient with reduced complaints, and there was no *Candida* in the repeated vaginal culture performed on the third day of treatment. The patient was discharged after two weeks of treatment. She used vaginal ovule containing *Lactobacillus acidophilus* and oestriol for six months and had no recurrence after one year of follow-up.

### Discussion

*Candida albicans* is the most common agent responsible for up to 90% of vaginal candidiasis and is usually susceptible to antifungals (Donders et al. 2010). Azole-susceptible non-*albicans* strains takes in second place (Donders et al. 2010; Marchaim et al. 2012). Turkey also has similar resistance rates with the world. In a study (Güzel et al. 2013), antifungal susceptibilities of 216 vulvovaginitis causing *C. albicans* strains evaluated and azole resistance was observed in only two isolates.

Vulvovaginal candidiasis negatively affects the daily life of patients and their sexual partners. Most acute attacks are treated empirically by the patients themselves or by physicians. Fluconazole—containing topical treatments (ovules, creams, etc.) and the systemic drugs—are being used often for this purpose. An oral single dose of 150 mg fluconazole or 100 mg oral itraconazole twice a day are the main treatment options for the treatment of acute vulvovaginal candidiasis. There are also topical treatment options including amphotericin B, nystatin, miconazole, clotrimazole or

flucytosine (van Schalkwyk et al. 2015; Workowski and Bolan 2015). A prolonged, 7–30 days of treatment may be required, especially for recurrent candidiasis. There are also publications indicating that boric acid-containing capsules may be useful for non-albicans strains (Sobel and Sobel 2018; Felix et al. 2019). Despite all of these regimens, recurrent vulvovaginitis may still be a common problem for women.

Clinical response is high with many of these antifungal agents (especially azole derivatives) which are commonly used in vaginitis, but recurrence is common. In the presence of recurrent infection, various risk factors such as anatomical features, antibiotic use, impaired glucose metabolism, use of oral contraceptives, and immunosuppression should be investigated, while the patient should be warned about diet regulation, increasing genital hygiene and avoiding too tight or synthetic underwear (Donders et al. 2010).

The patients with no response can be treated with suppressive treatment regimens including the use of oral or vaginally administered azole derivatives (Sobel 2016). Nevertheless, it should be kept in mind that azole resistant *Candida* may be responsible in patients who do not respond to treatment, even if there is no risk factor. As seen in this case, *C. albicans* may rarely cause infections resistant to not only fluconazole, but also itraconazole and voriconazole. Hence, antifungal sensitivity tests are necessary for the treatment success of the recurrent or refractory superficial fungal infections treatment. Topical options, such as boric acid, nystatin and amphotericin B, are recommended in the treatment of azole-resistant *Candida* vaginitis in the literature, but these agents are not available in Turkey.

Although there are papers suggesting the administration of systemic caspofungin for such cases, to our knowledge there is no case report related to anidulafungin (Karabay et al. 2018). To the best of our knowledge, this is the first fluconazole-itraconazole-voriconazole-resistant *C. albicans* vaginitis case reported from Turkey, as well as world, and the first case of vaginitis treated with anidulafungin.

## Conclusion

*C. albicans* is commonly known as being susceptible to all antifungal drugs but it should be kept in mind that resistant strains may be responsible for the infections for recurrent

and unresponsive vulvovaginal candidiasis cases. For this reason, antifungal susceptibility tests are necessary for treatment success in the cases of recurrent and non-response to treatment. Although there is no case report in which anidulafungin is used for treatment, it should be kept in mind that the anidulafungin may be used as salvage treatment.

## Disclosure statement

All authors have no conflicts of interest to declare.

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## References

- Clinical and Laboratory Standards Institute. 2008. Reference method for broth dilution antifungal susceptibility testing of yeasts; Approved Standard – Third Edition. M27–A3. Vol. 28. Wayne, PA: Clinical and Laboratory Standards Institute.
- Donders GG, Bellen G, Mendling W. 2010. Management of recurrent vulvo-vaginal candidosis as a chronic illness. *Gynecologic and Obstetric Investigation* 70:306–321.
- Felix TC, de Brito Röder DVD, dos Santos Pedrosa R. 2019. Alternative and complementary therapies for vulvovaginal candidiasis. *Folia Microbiologica* 64: 133–141.
- Güzel AB, Döğen A, Aydın M, Serin A, Serin MS, Kalkancı A, et al. 2013. Genotyping reveals no link between *Candida albicans* genotype and vaginitis severity in Turkish women. *Mycopathologia* 175:287–294.
- Karabay O, Bastug A, Ozturk R, Sencan I, Aksoy M, Simsek H, et al. 2018. Antibiotic Consumption, Resistance Data, and Prevention Strategies. *Mediterranean Journal of Infection, Microbes and Antimicrobials* 7:35.
- Marchaim D, Lemanek L, Bheemreddy S, Kaye KS, Sobel JD. 2012. Fluconazole-Resistant *Candida albicans* Vulvovaginitis. *Obstetrics and Gynecology* 120: 1407–1414.
- Sobel JD. 2016. Recurrent vulvovaginal candidiasis. *American Journal of Obstetrics and Gynecology* 214:15–21.
- Sobel JD, Sobel R. 2018. Current treatment options for vulvovaginal candidiasis caused by azole-resistant *Candida* species. *Expert Opinion on Pharmacotherapy* 19:971–977.
- van Schalkwyk J, Yudin MH, Yudin MH, Allen V, Bouchard C, Boucher M, et al. 2015. Vulvovaginitis: Screening for and Management of Trichomoniasis, Vulvovaginal Candidiasis, and Bacterial Vaginosis. *Journal of Obstetrics and Gynaecology Canada* 37:266–274.
- Workowski KA, Bolan GA; Centers for Disease Control and Prevention. 2015. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recommendations and Reports* 64:1–137.