Clinical, Cosmetic and Investigational Dermatology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

Diagnostic Challenge: Prolonged Misdiagnosis of Perianal Herpes in an Immunosuppressed Transplant Patient

Xinze Li[1–5,*], Weijun Liu[1–5,*], Lifang Cheng[1–5], Xiaohua Tao[1–5], Jing Zhang[1–5]

[1]Department of Dermatology, Dermatology Hospital of Jiangxi Province, Nanchang, Jiangxi, People's Republic of China; [2]Department of Dermatology, Jiangxi Provincial Clinical Research Center for Skin Diseases, Nanchang, Jiangxi, People's Republic of China; [3]Department of Dermatology, Candidate Branch of National Clinical Research Center for Skin Diseases, Nanchang, Jiangxi, People's Republic of China; [4]Department of Dermatology, Dermatology Institute of Jiangxi Province, Nanchang, Jiangxi, People's Republic of China; [5]Department of Dermatology, The Affiliated Dermatology Hospital of Nanchang University, Nanchang, Jiangxi, People's Republic of China

*These authors contributed equally to this work

Correspondence: Jing Zhang; Xiaohua Tao, Department of Dermatology, Dermatology Hospital of Jiangxi Province, Nanchang, Jiangxi, 330000, People's Republic of China, Tel +86 19855134654, Fax +86-0791-85207512, Email jzhang_pf@163.com; taoxiaohua@126.com

Abstract: Perianal herpes simplex virus (HSV) infection represents a rarely reported clinical variant that is frequently misdiagnosed. We present a case of perianal HSV in a patient with a history of renal transplantation and type 2 diabetes mellitus. Following a previous diagnosis of perianal eczema, the patient's cutaneous lesions slowly worsened despite treatment with topical corticosteroids. Notably, the presence of well-demarcated superficial erosions, combined with immunosuppressive conditions including diabetes mellitus and renal transplantation, prompted targeted HSV screening which confirmed the diagnosis. This case underscores the importance of considering HSV testing in patients presenting with atypical perianal eruptions.

Keywords: herpes simplex virus, misdiagnosis, renal transplantation, diabetes mellitus

Introduction

Genital herpes is a common sexually transmitted infection caused by herpes simplex virus (HSV), predominantly HSV-2.[1] The virus infects and replicates in epithelial cells, leading to vesicle formation, and subsequently establishes latency in neuronal ganglia until reactivated by various triggers.[2] While the genitalia are the most commonly affected sites, infections may also involve the perineum, buttocks, upper thighs, or perianal region. Clinical manifestations range from solitary or clustered vesicles, pustules, and erosions to ulcers. Atypical presentations are not uncommon, particularly in immunocompromised individuals. HSV infection poses a significant clinical challenge in solid organ transplant recipients, potentially increasing morbidity and mortality while impacting graft survival; post-transplant immunosuppressive medications substantially elevate the risk of HSV infection.[3] Herpes simplex virus infections in immunocompromised patients may present with atypical morphologies. In post-transplant individuals, clinical manifestations including verrucous, minimally exudative and intensely painful plaques, as well as genital mass-like lesions have been documented.[4,5] Additionally, type 2 diabetes mellitus represents a significant risk factor for genital and perianal HSV infections.[6] Herein, we report a case of perianal HSV infection in a renal transplant recipient with pre-existing type 2 diabetes.

Case Presentation

A 51-year-old male presented with a three-month history of perianal erythema, erosions, pruritus, and pain. He reported no previous episodes of vesicles or erosions in the genital or perianal regions and denied systemic symptoms such as fever or malaise. Prior treatment for suspected eczema, including topical corticosteroids and intravenous anti-inflammatory agents, had yielded no significant improvement. His medical history included a right renal transplant performed six years earlier.

Received: 7 October 2025
Accepted: 27 November 2025
Published: 3 December 2025

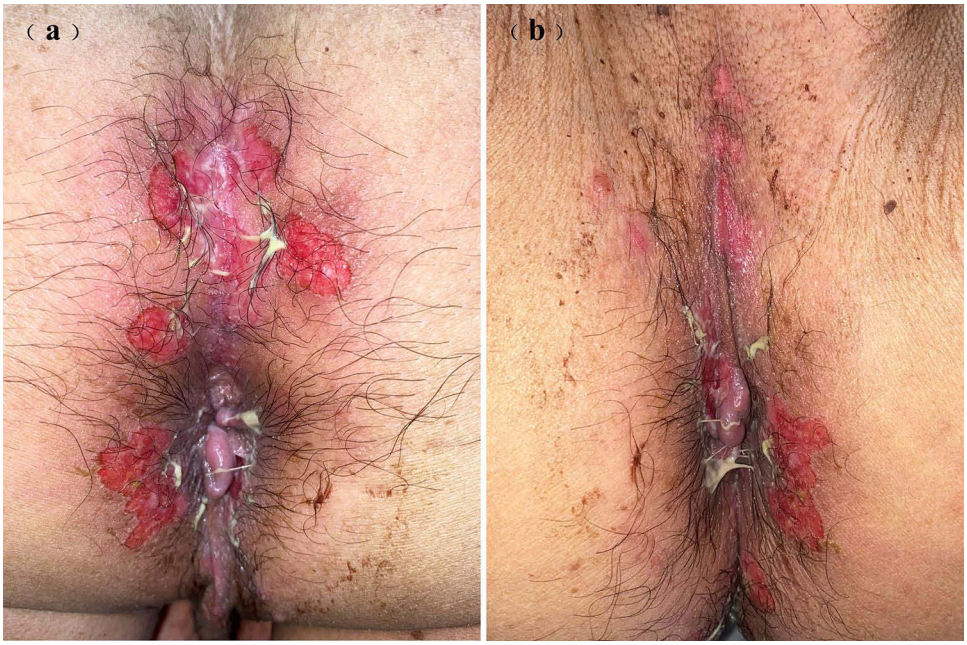

Figure 1 Pretreatment Clinical Images of Anogenital Region. (**a**) Multiple Well Circumscribed Round Erosions in Perianal Region Prone Position; (**b**) Multiple Well Circumscribed Round Perianal Erosions with Right Sided Vesicle in Supine Position.

His current immunosuppressive regimen consisted of cyclosporine 100mg twice daily and prednisone 5mg once daily. He also had a six-year history of type 2 diabetes mellitus, managed with subcutaneous insulin glargine 30 IU nightly and insulin aspart 20 IU before each meal. Physical examination revealed multiple, densely distributed, round erythematous lesions with superficial erosions and minimal exudate in the perianal area, ranging in size from soybean to nail-cap, with relatively well-defined borders. A millet-sized vesicle was observed superior and lateral to the anus with the patient in the supine position (Figure 1). The observation of perianal erosions and vesicles raised the suspicion of pemphigus vegetans, warranting appropriate screening. Additionally, the patient's medical history—including diabetes mellitus, renal transplantation, and long-term immunosuppressive therapy with corticosteroids and cyclosporine post-transplantation—indicated a significantly immunocompromised status. The combination of these factors, particularly the presence of well-demarcated, round, superficial erosions, strongly suggested the need for herpes simplex virus (HSV) testing. Concurrently, histopathological examination was conducted to rule out perianal tuberculosis and Crohn's disease. Laboratory investigations were negative for HSV-1 DNA, desmoglein (Dsg)1, Dsg3, bullous pemphigoid (BP)180 antibodies, lymphocyte function tests, syphilis, and HIV. Histopathological examination of a perianal erosion showed focal epidermal necrosis with crusting, hyperkeratosis, parakeratosis, mild acanthosis, slight spongiosis and intracellular edema, swelling of superficial dermal vascular endothelial cells, and a scattered inflammatory infiltrate composed predominantly of neutrophils and lymphocytes, accompanied by occasional multinucleated giant cells. Direct immunofluorescence was negative (Figure 2). Bacterial culture from the erosions yielded *Klebsiella pneumoniae* and *Morganella morganii*. PCR testing confirmed the presence of HSV-2 DNA from the perianal lesions. The patient was started on valacyclovir hydrochloride 0.5g orally twice daily. Complete re-epithelialization of the lesions was observed after eight days of antiviral therapy (Figure 3).

Discussion

Sexual transmission represents the primary route for HSV-2 dissemination, with established risk factors including female sex, age, number of sexual partners, and HIV co-infection. Additionally, vertical transmission may occur when neonates are exposed to infected genital secretions in utero or during delivery.[7]

The clinical presentation of genital herpes typically includes solitary or grouped vesicles affecting the genitalia, perineum, buttocks, upper thighs, or perianal region. Beyond this classic morphology, cases of HSV infection manifesting

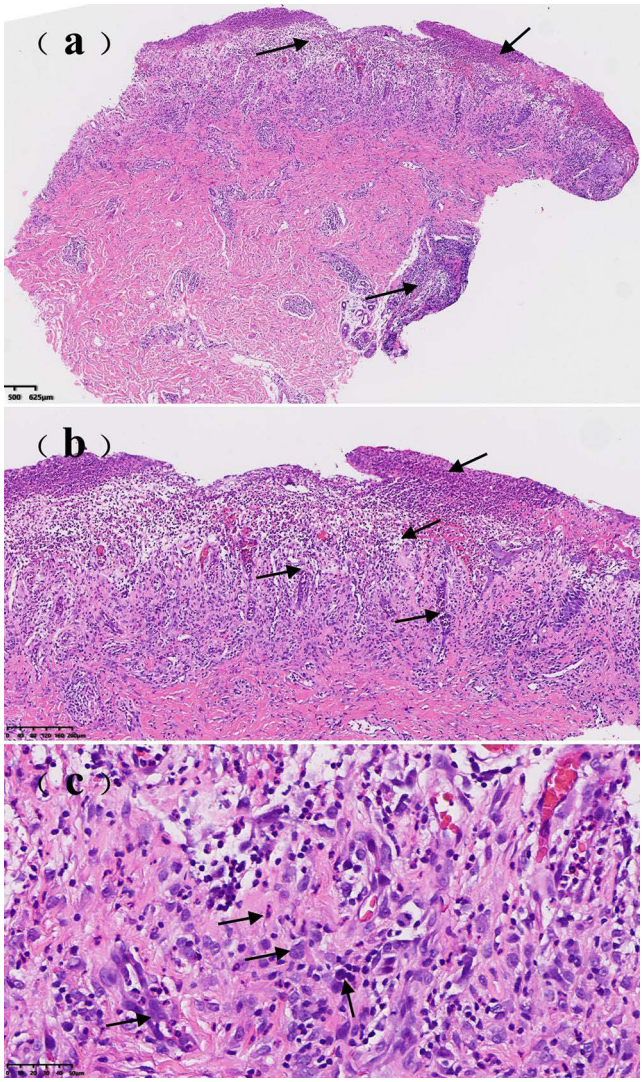

Figure 2 Histopathological image of the skin lesion on the Perianal Erosions. (**a**) Epidermal necrosis with inflammatory cell infiltration surrounding dermal vessels and adnexa (HE×40); (**b**) Abundant serocrust deposition, vascular proliferation in superficial dermis, and dense inflammatory infiltrate (HE×100); (**c**) Swollen vascular endothelium in dermis with mixed inflammatory infiltrate of neutrophils, lymphocytes, and histiocytes (HE×400).

as extensive perianal ulcerations have been documented.[8] Additionally, perianal herpes simplex infection mimicking cutaneous neoplasms has been reported in patients with AIDS.[9]

Immunocompromised individuals may develop hypertrophic herpes genitalis (HHG), an uncommon anogenital variant. A review of the literature identified 24 reported cases of HHG, 23 of which occurred in individuals infected with the human immunodeficiency virus (HIV).[10] Beyond HIV, hypertrophic perianal herpes simplex virus infection has also been observed in renal transplant recipients.[11] Apart from hypertrophic plaques, atypical clinical presentations such as tumor-like nodules or condyloma-like lesions have also been described in published reports.[9]

Differential diagnoses should include the following conditions. Perianal herpes is most frequently misdiagnosed clinically as perianal eczema. The conventional use of corticosteroids in eczema management can potentially exacerbate and prolong the disease course. In our case, the erosions were relatively superficial, contrasting with the lichenified or hyperkeratotic plaques typical of chronic eczema. Another significant entity to consider is perianal tuberculosis, which may present with local pain, mucopurulent discharge, and multiple complex anal fistulas. Histopathology typically demonstrates ulcerations surrounded by non-specific inflammatory infiltrates with extensive caseous necrosis.[12] The presence of a vesicle on the right perineum, combined with perianal erosions, creates clinical similarities to pemphigus

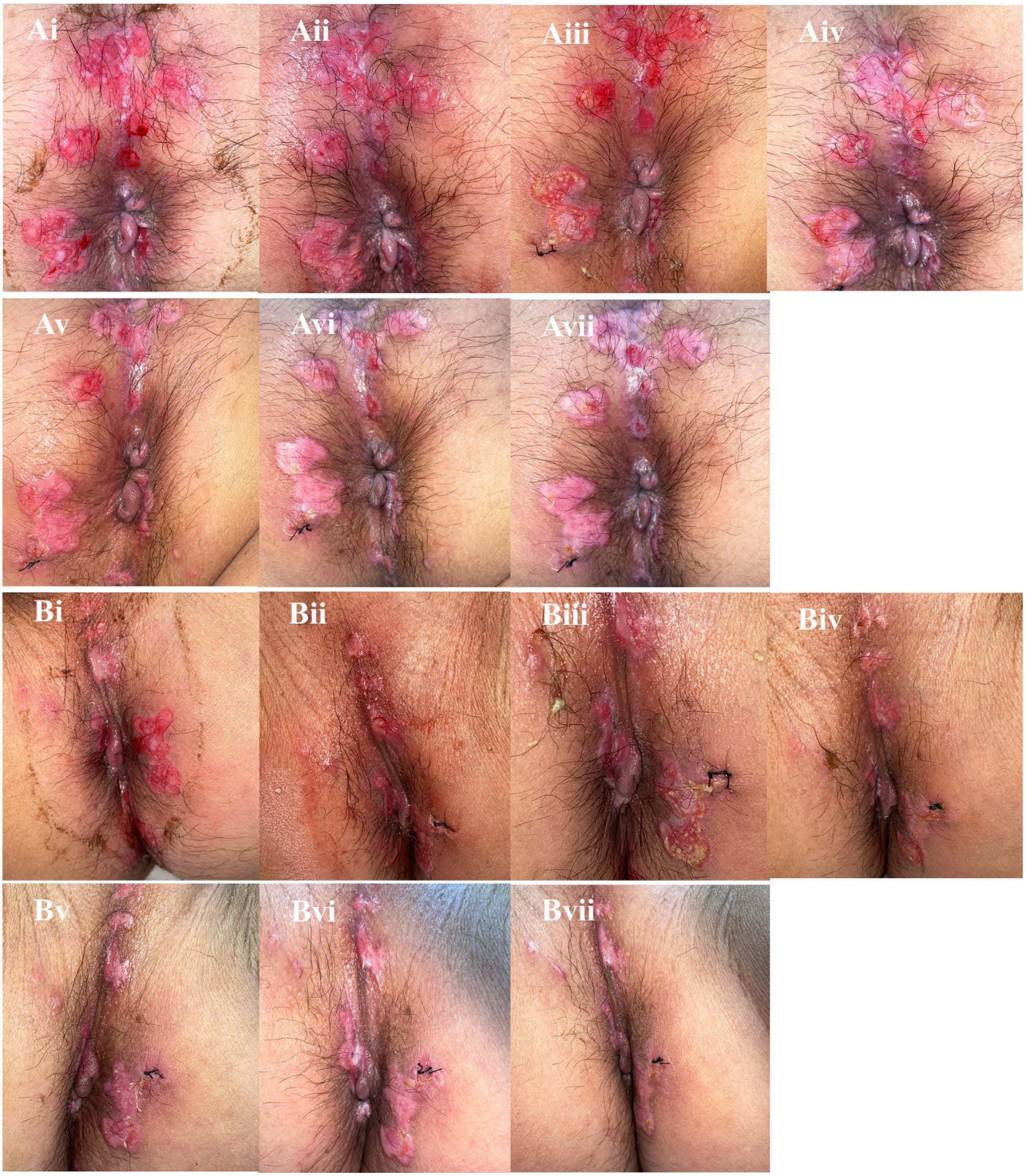

Figure 3 Clinical Images of the Anogenital Region during the treatment. (**Ai–Avii**) Daily Resolution of Perianal Lesions from Day 1 to 7 Post-Treatment in Prone Position; (**Bi–Bvii**) Daily Healing of Perianal Lesions Days 1 to 7 Posttreatment Supine Position.

vegetans and Hailey-Hailey disease.[13,14] However, our patient tested negative for both Dsg1 and Dsg3 antibodies, and neither routine histology nor immunopathology revealed features indicative of these conditions. This condition also requires differentiation from cutaneous metastatic Crohn's disease (MCD). MCD can manifest as genital edema, induration, skin tag-like lesions, nodules, or fissures. Histopathological examination typically shows non-caseating granulomas.[15] Pyoderma gangrenosum (PG) represents another important differential diagnosis. PG is a rare neutrophilic

dermatopathy, with the ulcerative subtype being most common, characterized by painful, well-demarcated ulcers.[16] Notably, a case has been reported of perianal HSV-1 infection in an immunosuppressed patient presenting as a large ulcer initially misdiagnosed as PG.[17]

The development of this case was attributed to two primary predisposing factors: renal transplantation and type 2 diabetes mellitus. It has been documented in the literature that atypical presentations of HSV-induced genital masses are not limited to HIV-infected patients but may also occur in other immunocompromised populations, such as organ transplant recipients.[5] While HSV-2 generally causes less severe infections in transplant recipients, a case of rapidly disseminated cutaneous HSV-2 infection with meningoencephalitis has been reported three months post-transplantation.[18] Type 2 diabetes contributes to immunodeficiency through insulin deficiency and hyperglycemia, which collectively suppress cytokine production, impair phagocytosis, lead to dysfunctional immune cells, and compromise microbial clearance. Studies have shown that deteriorated glycemic control is associated with increased incidence of bronchitis, pneumonia, skin and soft tissue infections, urinary tract infections, and genital and perianal infections, whereas no such association was found with upper respiratory infections, influenza-like illness, or enteric infectious diseases.[6]

Klebsiella pneumoniae and *Morganella morganii* are both opportunistic Gram-negative pathogens.[19,20] Cutaneous infections caused by K. pneumoniae primarily occur in individuals with compromised host defense, such as those with diabetes mellitus, malignancy, corticosteroid therapy, or renal failure.[21] Infections with *M. morganii* can affect patients of any age.[20] Literature indicates that *K. pneumoniae* is among the most frequently isolated organisms in such contexts.[20] Given that both organisms likely represent secondary superinfection following erosions from primary HSV infection and impaired skin barrier function, compounded by long-term topical corticosteroid use, our patient did not receive targeted antibacterial therapy. Notably, the withholding of targeted antibacterial therapy for these two secondary bacterial infections did not compromise the eventual healing of the local skin lesions.

The patient's perianal erosions were repeatedly misdiagnosed, resulting in a protracted HSV disease course of three months. The persistent perianal lesions caused significant ambulatory discomfort and substantially compromised the patient's quality of life. In this case, we meticulously documented the daily resolution of the cutaneous lesions following appropriate therapy with serial clinical photographs. While genital vesicles or erosions typically prompt clinicians to consider herpes simplex infection, isolated perianal manifestations can easily lead to overlooking the diagnosis of anogenital herpes. The generalizability of our findings is limited by the nature of a single case report. Further studies with larger cohorts are warranted to fully characterize the clinical spectrum of this condition.

Conclusion

In conclusion, the presentation of perianal erosions or vesicles in immunosuppressed individuals should raise strong clinical suspicion for herpes simplex virus infection. Heightened awareness is essential to prevent prolonged misdiagnosis, disease progression, and unnecessary extension of the clinical course.

Abbreviations

HSV, herpes simplex virus; HHG, hypertrophic herpes genitalis; HIV, human immunodeficiency virus; Dsg, desmoglein; MCD, metastatic Crohn's disease; PG, pyoderma gangrenosum; BP, bullous pemphigoid.

Ethics Statement

The patient provided written informed consent for publication of this report and accompanying images. The Ethics Committee of Jiangxi Provincial Dermatology Hospital, has approved the publication of the case details.

Acknowledgments

These authors contributed equally to this work. Xinze Li and Weijun Liu are the first co-authors of this study.

Funding

There is no funding to report.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Wald A, Ewell MG, Wolff PA, et al. Epidemiology, clinical presentation, and antibody response to primary infection with herpes simplex virus type 1 and type 2 in young women. *Clin Infect Dis*. 2013;56(3):344–351. doi:10.1093/cid/cis891
2. Saleh D, Yarrarapu SNS, Sharma S. Herpes simplex type 1. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2025.
3. Fishman JA. Infection in organ transplantation. *Am J Transplant*. 2017;17:856–879. doi:10.1111/ajt.14208
4. Boix-Vilanova J, Montis MC, Giacaman A, et al. Herpes vegetans in a human immunodeficiency virus-negative kidney transplant patient. *Clin Exp Dermatol*. 2019;44(1):92–94. doi:10.1111/ced.13748
5. Hanjani NM, Foster DC, Scott GA, et al. A genital mass due to herpes simplex virus in a renal transplant recipient. *J Low Genit Tract Dis*. 2007;11(3):173–176. doi:10.1097/LGT.0b013e31802f3142
6. Hine JL, de Lusignan S, Burleigh D, et al. Association between glycaemic control and common infections in people with type 2 diabetes: a cohort study. *Diabet Med*. 2017;34(4):551–557. doi:10.1111/dme.13205
7. Sacks SL, Griffiths PD, Corey L, et al. HSV-2 transmission. *Antiviral Res*. 2004;63(Suppl 1):S27–35. doi:10.1016/j.antiviral.2004.06.005
8. Sirka CS. Clinical features of a large chronic ulcer on the genital and perianal region in HIV-infected patients can be a strong clinical clue for the diagnosis of herpes simplex infection. *Indian J Sex Transm Dis AIDS*. 2020;41(2):192–195. doi:10.4103/ijstd.IJSTD_140_15
9. Mosunjac M, Park J, Wang W, et al. Genital and perianal herpes simplex simulating neoplasia in patients with AIDS. *AIDS Patient Care STDS*. 2009;23(3):153–158. doi:10.1089/apc.2008.0143
10. Strehl JD, Mehlhorn G, Koch MC, et al. HIV-associated hypertrophic herpes simplex genitalis with concomitant early invasive squamous cell carcinoma mimicking advanced genital cancer: case report and literature review. *Int J Gynecol Pathol*. 2012;31(3):286–293. doi:10.1097/PGP.0b013e318237d581
11. Trevisan G, Germi L, Dissegna D, Famengo B. Hypertrophic perianal Herpes simplex in renal transplant recipient. *G Ital Dermatol Venereol*. 2017;152(5):547–548. doi:10.23736/S0392-0488.16.05377-3
12. Takahashi AAR, Bassaneze T, Longo KS, et al. Primary extensive perianal cutaneous tuberculosis: a challenging diagnosis. Case report and a review of the literature. *Braz J Infect Dis*. 2023;27(1):102722. doi:10.1016/j.bjid.2022.102722
13. Kluger N, Mandelin J, Lappalainen K. Pemphigus végétant périanal [Perianal pemphigus vegetans]. *Presse Med*. 2016;45(10):945–946. French. doi:10.1016/j.lpm.2016.05.013
14. Rogner DF, Lammer J, Zink A, et al. Darier and Hailey-Hailey disease: update 2021. *J Dtsch Dermatol Ges*. 2021;19(10):1478–1501. doi:10.1111/ddg.14619
15. Ickrath F, Stoevesandt J, Schulmeyer L, et al. Metastatic Crohn's disease: an underestimated entity. *J Dtsch Dermatol Ges*. 2021;19(7):973–982. doi:10.1111/ddg.14447
16. Maverakis E, Marzano AV, Le ST, et al. Pyoderma gangrenosum. *Nat Rev Dis Primers*. 2020;6(1):81. doi:10.1038/s41572-020-0213-x
17. Saunderson RB, Tng V, Watson A, et al. Perianal herpes simplex virus infection misdiagnosed with pyoderma gangrenosum: case of the month from the case consultation committee of the international society for the study of vulvovaginal disease. *J Low Genit Tract Dis*. 2016;20(2):e14–5. doi:10.1097/LGT.0000000000000178
18. Truffot A, Noble J, Dartevel A, et al. Fatal HSV-2 primary infection most likely acquired by kidney transplantation: a case report. *Int J Antimicrob Agents*. 2023;61(5):106769. doi:10.1016/j.ijantimicag.2023.106769
19. Wang G, Zhao G, Chao X, et al. The characteristic of virulence, biofilm and antibiotic resistance of Klebsiella pneumoniae. *Int J Environ Res Public Health*. 2020;17(17):6278. doi:10.3390/ijerph17176278
20. Alsaadi A, Alghamdi AA, Akkielah L, et al. Epidemiology and clinical characteristics of Morganella morganii infections: a multicenter retrospective study. *J Infect Public Health*. 2024;17(3):430–434. doi:10.1016/j.jiph.2023.12.013
21. Hu T, Wang M, Chen W, et al. The clinical characteristic and outcome of skin and soft tissue infection in immunosuppressive patients with nephrotic syndrome. *Clin Exp Nephrol*. 2020;24(9):779–788. doi:10.1007/s10157-020-01893-w