

Case report: Successful treatment of Candidal granuloma caused by *Candida parapsilosis* with oral fluconazole and terbinafine

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Summary

Candidal granuloma is a rare disease and treatment is still difficult in clinical practice. This disease is common in immunocompromised patients. Herein, we report a case of a 63-year-old man who presented with Candidal granuloma caused by *Candida parapsilosis*. The diagnosis was confirmed according to fungal culture. The patient was successfully treated with oral fluconazole and terbinafine. After 2 months, the skin lesions were fully resolved and after 6 months of follow-up, there was no recurrence.

Keywords: *Candida parapsilosis*, Candidal granuloma, fluconazole, terbinafine.

I. BACKGROUND

In recent years, *Candida parapsilosis* has emerged as a leading non-albicans species, with a significant increase in its isolation⁹. In reality, there are not many case reports of Candidal granuloma - a rare type of cutaneous candidiasis, manifesting as erythematous, inflammatory papules, nodules, blisters, pustules, abscesses, and scaly plaques involving the skin, mucous membranes, nails, and commonly affecting the face, scalp, hands, and trunk⁵. Diagnosis and treatment of this rare disease remain challenging. Herein, we report a case of primary cutaneous fungal infections caused by *C. parapsilosis* successfully treated with a multimodality approach, including topical and systemic antifungal therapy (fluconazole + terbinafine) and antihistamines.

II. CASE PRESENTATION

A 63-year-old male with no past medical history, presented with a 1-centimeter, firm, erythematous papule with a raised, smooth surface and a well-defined border on the right cheek, accompanied by severe pruritus. Dermoscopic manifestation of the papule revealed telangiectasia and scales on an erythematous base. The patient sought medical attention at hospital X and was initially diagnosed with allergic contact dermatitis based on clinical symptoms and examination of dermoscopy. He was treated with oral antihistamine, topical corticosteroids (Fucicort) and topical tacrolimus, with no improvement.

After 2 months, the patient presented to our department with an enlarged skin lesion of 4cm plaque with numerous papules of 2-3mm in the diameter at the periphery of this lesion on the right side of the cheek (figure 2). Microscopic examination revealed no evidence of fungal infection. A skin biopsy showed mild hyperkeratosis, the presence of mononuclear cell infiltrates in the dermis, and no evidence of malignancy. A diagnosis of Granuloma annulare was made based on clinical picture, consequently, oral antihistamine and topical

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Fucicort twice daily were continued. However, in 2 days pustules rapidly appeared on the surface of the lesion and fungal culture of the pustules was negative. The patient was treated with oral cefixime 200mg twice daily as a prophylactic measure against bacterial infections. After 7 days, a few papules remained at the periphery of the lesion, and the central lesion remained unchanged (figure 1). Once again, a fungal culture of the pustules was taken from the lesion site and was examined at another facility, which revealed *Candida parapsilosis*. The

patient was subsequently treated with oral fluconazole 200mg once weekly and oral ebastine once daily. Follow-up after 2 weeks showed mild improvement, thus the decision was made to add oral terbinafine 250mg once daily for 1 week to the treatment, as well as oral ebastine 10mg once daily and topical ciclopirox olamine twice daily for 2 weeks. A complete resolution of skin lesions was observed after 4 weeks, and there were no signs of recurrence for the subsequent 6 months (figure 1, 2).

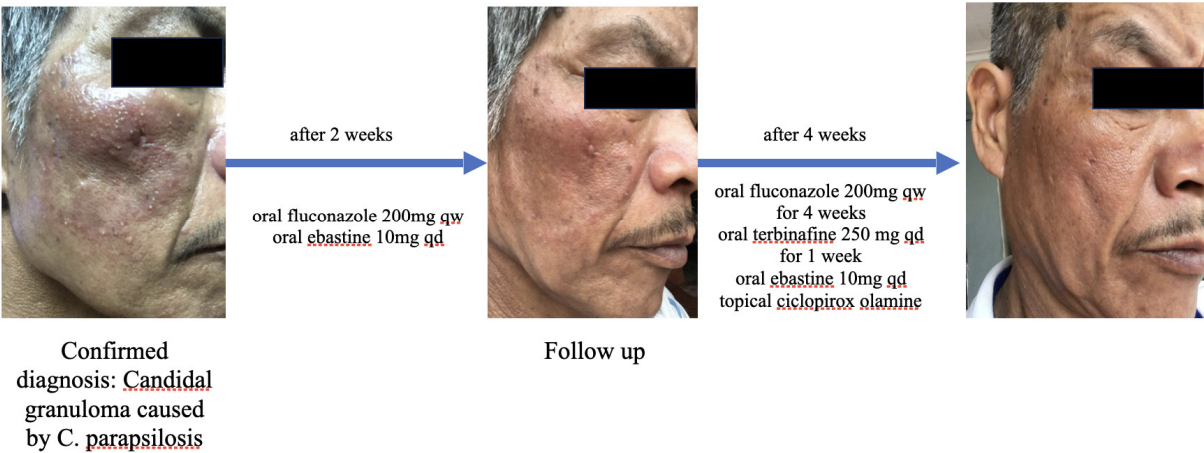


Figure 1. Detailed time course of the patient's clinical course and therapeutic regimen



Figure 2. Skin lesions before and after treatment with follow-up

III. DISCUSSION

Candida spp. is an opportunistic pathogen, having been isolated from domestic animals, soil, insects and marine environment¹⁷. However it can also be found in human skin, mucosa and nails,

causing local infections of these sites, and possibly systemic infection with dissemination of the disease⁷. The SENTRY Antimicrobial Surveillance Programme reported that during the last few decades, the spectrum of infections has undergone a drastic change¹². Although *Candida albicans* is the

most common pathogenic fungal type of infection, non-albicans *Candida* have emerged as an important cause of infections. The prevalence of *Candida albicans* infections is decreasing by year, while the prevalence of non-albicans infections, including *Candida parapsilosis*, is increasing in a proportional way¹¹. Despite the fact that the incidence of candida infection, including *C. parapsilosis*, is rising dramatically along with other pathogens due to the wide use of broad-spectrum antibiotics, glucocorticoids, immunosuppressive drugs and invasive medical devices such as central venous catheter, *C. parapsilosis* cutaneous infection is considered to be rare¹. Wu J, et al., 2021 reviewed 10 cases of *C. parapsilosis* cutaneous infection¹⁸. In which onychomycosis is the most prevalent clinical type of *C. parapsilosis* manifestation^{3,4,8,10,14,15,18}. Three cases reported subcutaneous candidiasis, which include deep-seated subcutaneous ulcer on the right shoulder, wart-like nodules on the planta and subcutaneous ulcer on the right leg^{6,18,19}.

Hauser and Rothman (1950) reported the first case of *Candida* granuloma, which is a rare type of deep cutaneous candidiasis, characterized by the presence of papules, nodules, blisters, pustules, abscesses and plaques covered with thick yellow-brown scabs, commonly affected the face, scalp and trunk of infants, children and immunocompromised individuals or those using immunosuppressants⁵. *C. parapsilosis* mainly causes superficial infections such as onychomycosis, vulvovaginitis, and systemic infections such as fungemia, endocarditis meningitis, and peritonitis¹⁶. Candidal granuloma caused by *C. parapsilosis* is considered to be an uncommon disease and it is hard to diagnose and treat in clinical practice. The most common cause of granuloma is infection, such as bacterial or fungal. In our case, the patient was incorrectly diagnosed twice as allergic contact dermatitis and granuloma annulare, leading to the wrong treatment strategy. Firstly, when there was no adequate response to antibiotics, we need to think about other etiology that cause the disease, such as fungal infection. Thus, it is important to know differential diagnosis for granuloma-like lesions.

Díaz-García J et al (2022) reported that echinocandin susceptibility in *C. parapsilosis* remained consistent, however, a notable increase in fluconazole resistance was observed, particularly in *C. parapsilosis* isolates, with rates rising from 2.6% in 2019 to 36.6% in 2022². Consequently, the treatment of *C. parapsilosis* infections is still significantly challenging. First-choice treatment of Candidal granuloma is systemic antifungal medication. However, as said above, fluconazole resistance was observed in *C. parapsilosis* isolates, therefore administering a combination of antifungal drugs was a safe choice. Combination of fluconazole with terbinafine acted synergistically on the ergosterol biosynthetic enzymes, which enhanced the efficacy of mycosis treatment by combining these two medications¹³. In this case, the patient had good response to fluconazole 200mg once weekly for 6 weeks combined with terbinafine 250mg once daily for 1 week, resulting in complete resolution of skin lesion and no recurrence after 6 months.

IV. CONCLUSION

In conclusion, candidal granuloma caused by *C. parapsilosis* is a rare disease. The incidence of fluconazole resistance in *Candida* spp. is rising, therefore the combination of oral fluconazole, terbinafine and topical antifungal medication seems to be a better choice over antifungal monotherapy for better response to the treatment. The patient's skin lesions subsided without any complication using the treatment combination and long-term follow-up for this patient showed no relapse.

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