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Resistant Oral Candidiasis in a Post-Radical Neck Dissection Patient: A Case Report

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ABSTRACT

Background: Oral candidiasis is a frequent opportunistic fungal infection in patients undergoing multimodal therapy for head and neck malignancies. Increasing azole resistance poses a significant therapeutic challenge and may lead to persistent lesions mistaken for tumor recurrence.

Case Presentation: We report a 73-year-old male with a history of radical neck dissection, radiotherapy, chemotherapy, and targeted therapy who presented with diffuse pseudomembranous plaques and severe xerostomia. Mycological culture identified Candida albicans resistant to fluconazole and itraconazole. The patient was treated with a short-course intravenous voriconazole regimen (200 mg once daily for five days), resulting in complete clinical resolution and improved oral comfort.

Discussion: Multimodal treatment for head and neck malignancy disrupts mucosal immunity and salivary gland function, predisposing patients to resistant fungal infection. Culture-guided antifungal selection is essential to prevent treatment failure. In this case, individualized voriconazole therapy demonstrated successful clinical response without systemic involvement, supporting the utility of targeted therapy in azole-resistant infections. However, further studies are necessary to validate this shortened dosing strategy.

Conclusion: Resistant oral candidiasis should be considered in post-treatment head and neck cancer patients with persistent mucosal lesions. Early microbiological confirmation and appropriate systemic antifungal therapy are critical for effective management and to avoid misdiagnosis as recurrence.

Keywords: oral candidiasis, azole resistance, voriconazole, radical neck dissection, chemotherapy, radiotherapy, xerostomia

INTRODUCTION

Oral candidiasis is the most common opportunistic fungal infection of the oral cavity, predominantly caused by *Candida albicans*, although infections by non-albicans species have increasingly been reported in recent years[1]. It is associated with predisposing conditions such as immunosuppression, xerostomia, mucosal injury, and prolonged antibiotic or corticosteroid therapy[2]. Patients who undergo treatment for suspected head and neck malignancy including radical neck dissection, radiotherapy, chemotherapy, or targeted therapy are particularly vulnerable due to impaired mucosal integrity, altered oral microbiota, and reduced salivary flow[3–6]. Clinically, oral candidiasis presents with pseudomembranous white plaques, glossodynia, dysgeusia, oral discomfort, and odynophagia[1].

Fluconazole remains the first-line therapy for oral candidiasis; however, resistance has increasingly emerged, including in patients undergoing multimodal therapy for head and

neck tumors[7,8]. Mechanisms contributing to resistance in C. *albicans* include ERG11 mutations and efflux pump overexpression, leading to therapeutic failure[9,10]. Voriconazole, a second-generation triazole, offers enhanced activity against resistant strains[8]. Nevertheless, reports of resistant oral candidiasis in post-radical neck dissection patients remain limited.

We present a case of fluconazole and itraconazole resistant oral candidiasis in an elderly male following radical neck dissection and multimodal therapy for suspected head and neck malignancy, successfully managed with a short-course intravenous voriconazole regimen.

CASE PRESENTATION

A 73-year-old male presented with a three-month history of persistent oral and throat discomfort described as a lump-like sensation. The symptoms developed after radical neck dissection followed by radiotherapy, chemotherapy, and targeted therapy for suspected head and neck malignancy. The patient also reported significant xerostomia. He was an active smoker with no comorbidities or relevant family history.

Physical examination revealed diffuse pseudomembranous white plaques involving the oral and oropharyngeal mucosa (Figure 1). Mycological culture and antifungal susceptibility testing of tongue and oropharyngeal swabs identified *Candida albicans* resistant to fluconazole and itraconazole but sensitive to ketoconazole and nystatin. Hematologic evaluation showed leukopenia and neutropenia, while liver and renal function were within normal limits.

The patient was diagnosed with resistant oral candidiasis and treated with intravenous voriconazole 200 mg once daily for five days, along with oral hygiene optimization. At two-week follow-up, clinical symptoms had resolved, xerostomia improved, and no plaques were observed on follow-up examination (Figure 2).

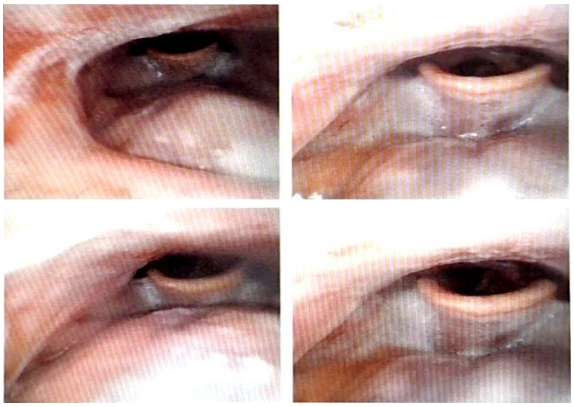

Figure 1. Diffuse pseudomembranous white plaques involving the oral and oropharyngeal mucosa prior to antifungal therapy.

Figure 2. Complete resolution of mucosal lesions after five days of intravenous voriconazole therapy.

The patient continued monthly follow-up for three months. He reported persistent viscous saliva, although no white plaques were observed. The patient was advised to maintain optimal oral hygiene and continue supportive xerostomia management.

DISCUSSION

Oral candidiasis commonly occurs in patients who have undergone multimodal therapy for suspected head and neck malignancy due to disruption of local immunity and salivary gland function[3–6]. Radical neck dissection may compromise parasympathetic innervation and vascular supply to major salivary glands, leading to reduced salivary flow and xerostomia[11]. Radiotherapy induces acinar cell destruction and fibrosis, while chemotherapy causes mucositis, suppresses epithelial regeneration, and alters the oral microbiome[3–6]. Certain targeted therapies may additionally impair epithelial barrier integrity and local immune responses depending on the inhibited

signaling pathway[5]. These cumulative effects promote Candida colonization and weaken mucosal host defense, as observed in the present patient.

Resistance to triazole antifungals in C. albicans has become an increasing challenge. Major mechanisms include ERG11 gene mutations altering the target enzyme lanosterol 14-α-demethylase and overexpression of efflux pumps such as CDR1, CDR2, and MDR1, which reduce intracellular antifungal accumulation. Biofilm-mediated tolerance further contributes to persistent infection and therapeutic failure[7–10].

Evidence based recommendations support the use of systemic antifungals in resistant or recurrent oral candidiasis, with voriconazole and posaconazole preferred due to their enhanced activity against azole-resistant isolates[7,8]. Echinocandins remain alternatives for refractory or invasive cases but are limited by cost, intravenous administration, and availability[8]. Supportive measures such as maintaining oral hygiene, managing xerostomia, and minimizing unnecessary antibiotics exposure are essential to reduce recurrence risk[2,6].

In this case, antifungal susceptibility testing guided the selection of voriconazole, resulting in complete clinical resolution despite a short, non-standard once-daily intravenous regimen for five days. Standard voriconazole regimens typically require twice-daily dosing and therapeutic drug monitoring; however, individualized decision-making based on resistance profile, patient frailty, and lack of systemic involvement enabled successful treatment.

This finding supports emerging evidence that culture-directed therapy improves clinical outcomes in antifungal-resistant infections. Nonetheless, as a single case without post-treatment microbiological confirmation, generalizability remains limited. Further clinical studies are needed to validate this shortened dosing strategy in similar high-risk populations.

This case highlights the importance for otolaryngologists to consider resistant candidiasis in post-treatment head and neck patients presenting with persistent mucosal lesions to prevent misdiagnosis as tumor recurrence and ensure prompt targeted antifungal therapy.

CONCLUSION

Resistant oral candidiasis should be considered in elderly patients who have undergone radical neck dissection and multimodal therapy for suspected head and neck malignancy, particularly when presenting with persistent mucosal plaques and xerostomia. Early microbiological confirmation and culture-guided systemic antifungal therapy are crucial to prevent treatment failure and diagnostic confusion with tumor recurrence. A short-course intravenous voriconazole regimen achieved effective clinical resolution in this case; however, further studies are required to validate its broader applicability. Continued optimization of oral hygiene and xerostomia management remains essential to reduce recurrence risk and improve patient outcomes.

Declaration by Authors

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