Olanzapine-Associated Oral Candidiasis in an Immunocompetent Patient: A Case for Further Investigation

Introduction:

Oral candidiasis, most commonly caused by *Candida albicans*, is a fungal infection of the oral cavity that frequently arises in the context of secondary immunosuppression. Clinically, it presents as white, curd-like patches or erythematous lesions on the tongue, palate, buccal mucosa, and tonsils. Oral thrush remains the most prevalent opportunistic infection among individuals living with HIV, serving as a clinical marker of immune dysfunction [1].

Beyond HIV, the incidence of oral candidiasis is also increased in conditions or treatments that impair immune function, such as chemotherapy, radiation therapy, hematologic malignancies like leukemia, and uncontrolled diabetes mellitus [2,3]. These risk factors underscore the central role of immune status in susceptibility to fungal infections.

Contextually, we report the case of an immunocompetent adult who developed oral candidiasis following treatment with olanzapine for psychosis. The patient had no prior history of immunosuppressive disorders, was not undergoing immunosuppressive therapy, and had no family history suggestive of immune dysfunction. Furthermore, the patient did not recall any previous episodes of oral candidiasis. This case raises the possibility of an underrecognized adverse effect of olanzapine, suggesting a potential immunomodulatory or immunosuppressive mechanism associated with the drug.

Antipsychotics such as olanzapine are not traditionally associated with immune compromise, emerging reports suggest their potential to influence immune parameters, including cytokine regulation and leukocyte function [4,5]. The case discussed in this case study highlights the need for further research into the immunological impact of antipsychotic medications, particularly in otherwise healthy individuals.

Case Presentation:

This study investigates the case of a 19-year-old male patient with a known history of paranoid schizophrenia who presented to the crisis stabilization unit due to exacerbation of psychotic symptoms, including delusions of grandiosity, manifesting as a belief that he is the "messiah." The patient reported non-compliance with his prescribed antipsychotic medication due to work-related stress. As a result, he experienced severe insomnia and appetite loss, causing a weight

reduction of 4 kg within the last 7 days. Previously, he was taking oral paliperidone 9 mg in the morning and 3 mg in the evening, stable on this for 3 years. Considering the severity of his symptoms and the need for rapid stabilization, we initiated treatment with olanzapine formulation at a starting dose of 10 mg.

Upon initiation of olanzapine therapy, the patient exhibited alleviation of psychotic symptoms, improved sleep, and enhanced functional ability. However, within the initial 24-hour period, the patient presented with tongue pruritus and discoloration symptoms. Subsequently, these symptoms extended to the mucous membranes, resulting in impaired mastication and phonation, accompanied by halitosis within the subsequent 48-hour period. The patient was admitted to the emergency department due to concerns about potential airway compromise. On examination, we found multiple white curd-like plaques on the tongue (Figure 1). Upon admission, he received a diagnosis of oral candidiasis and was suspected to have an immunocompromised condition. However, laboratory analysis revealed normal granulocyte and agranulocyte levels, as well as a normal range of leukocytes. The patient also had a negative result on the HIV test, ruling out immunodeficiency. Despite being a known diabetic, his diabetes was well managed with Metformin 500mg BD and Dapagliflozin 10 mg OD, and his HbA1C was within the reference range. The patient recalled a similar episode occurring 10 years prior when he was prescribed 10 mg of olanzapine for the management of his psychotic symptoms. The patient was advised to discontinue the medication immediately and was instructed to increase fluid intake. Upon cessation of the medication, the oral candidiasis resolved within 48 hours, suggesting olanzapine as the causal factor for oral thrush in an immunocompetent adult male.

Discussion:

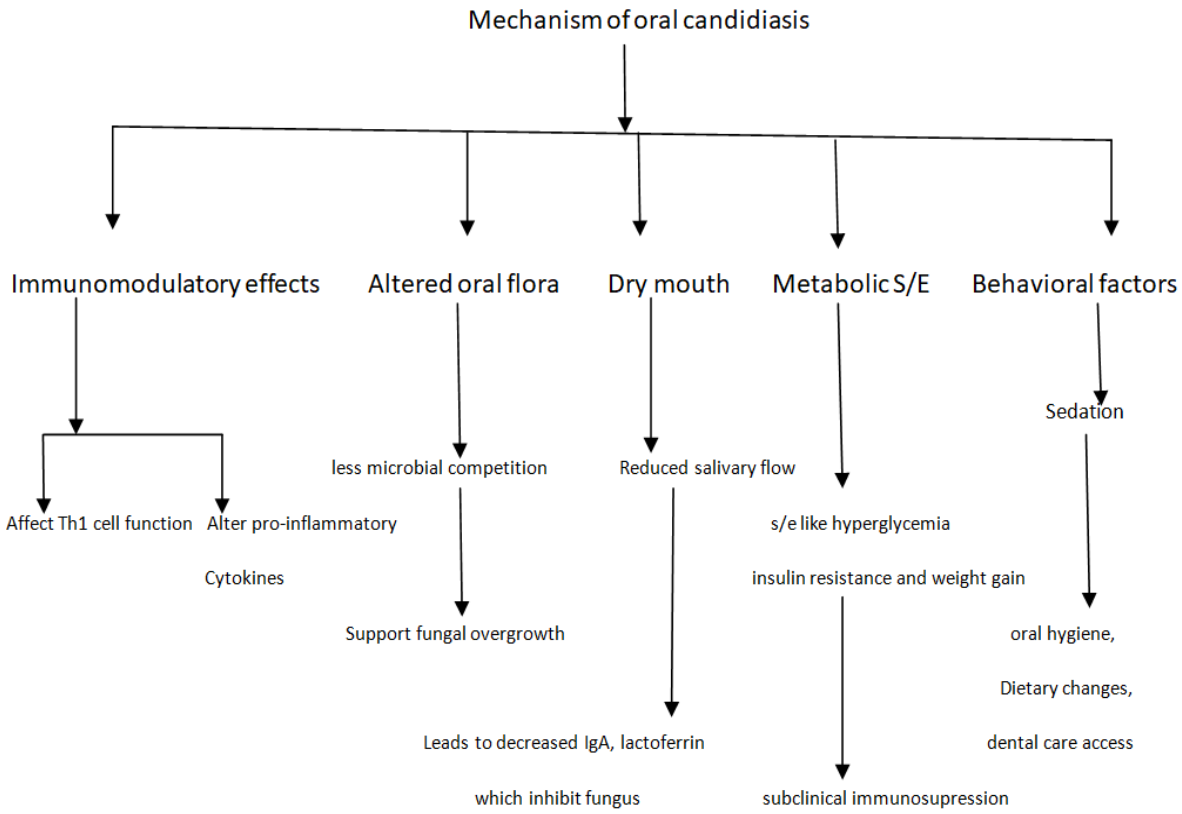
The manifestation of oral candidiasis as an adverse effect of oral olanzapine treatment in an immunocompetent patient is infrequent and underreported in the literature. Oral candidiasis, or thrush, is typically associated with immunocompromised conditions such as HIV/AIDS, poorly controlled diabetes mellitus, or the adverse effects of chemotherapy and corticosteroids– conditions in which mucosal immunity is impaired and Candida albicans can proliferate unchecked [1,2]. However, its emergence in individuals with no identifiable systemic immunodeficiency, such as in this case, necessitates the exploration of localized drug-induced mechanisms.

Oral candidiasis affects many adults, especially when systemic or local factors compromise mucosal defenses [3]. Our patient was thoroughly evaluated for common predisposing factors. HIV testing, white blood cell counts, and glycemic control (as indicated by HbA1c) were all within normal limits, indicating no overt immunosuppression. This clinical context raises the possibility that Olanzapine contributed to the fungal overgrowth.

Olanzapine is a second-generation antipsychotic with a high affinity for multiple receptor systems, including serotonergic (5-HT2A), dopaminergic (D2), histaminergic (H1), adrenergic (α1), and muscarinic (M1–M5) receptors [4]. Its antagonism of muscarinic receptors is especially relevant, as it often leads to xerostomia - a reduction in salivary flow. Saliva plays a vital role in oral defense, acting not only as a mechanical cleanser but also as a vehicle for antimicrobial proteins such as lysozyme, lactoferrin, histatins, and immunoglobulin A (IgA) [5]. Reduced saliva flow compromises these defenses, allowing *Candida albicans* to adhere to and invade mucosal surfaces (Table 1).

Xerostomia has also been shown to change oral pH and reduce the mechanical clearance of pathogens, further facilitating fungal colonization [6,7]. These mechanisms can operate independently of systemic immune status, suggesting that even in otherwise healthy individuals, pharmacologic xerostomia may predispose them to opportunistic infections like oral candidiasis (Table 1).

Moreover, olanzapine is well-documented to cause metabolic side effects, including weight gain, insulin resistance, and hyperglycemia- even in non-diabetic individuals [8]. Elevated salivary glucose levels, as seen in patients with diabetes or metabolic syndrome, provide an enriched environment for Candida growth [3]. This case highlights that even subtle or transient changes in



glucose regulation might increase susceptibility to fungal overgrowth (Table 1).

Table 1: Mechanism of Oral Candidiasis in patient taking olanzapine

In addition to their metabolic and anticholinergic effects, Olanzapine and other antipsychotics may have immunomodulatory properties, though they are not traditionally classified as immunosuppressants. Studies have shown that patients with schizophrenia, particularly those not receiving antipsychotics, may have elevated levels of pro-inflammatory cytokines such as IL-6, IL-2, and interferon-gamma [9,10]. Moreover, some antipsychotics have been shown to modulate cytokine expression and leukocyte function, potentially affecting local immune responses in mucosal tissues [11].

This case, therefore, underscores a critical but underrecognized point: oral candidiasis may be an adverse drug reaction to Olanzapine, even in immunocompetent individuals. The recurrence of

symptoms upon re-exposure to the same dose and the rapid resolution following discontinuation strengthen the causal association. While rare, this side effect should be on the clinician's radar, especially when initiating olanzapine therapy.

Preventive strategies include maintaining proper oral hygiene, encouraging hydration, using saliva substitutes, and monitoring for early symptoms of oral discomfort. In patients with a history of antipsychotic-associated xerostomia or candidiasis, clinicians should consider alternative agents with a lower anticholinergic burden.

Summary

Olanzapine is a second-generation antipsychotic used primarily in the treatment of schizophrenia and bipolar disorder. As seen in the case presentation, it has been associated with an increased risk of oral candidiasis. This presentation is mediated by Olanzapine's anticholinergic properties, which lead to reduced salivary secretion through the mechanism of antagonism of muscarinic receptors. Additionally, olanzapine-induced side effects such as weight gain, insulin resistance, and hyperglycemia may lead to a carbohydrate-rich environment in which Candida can grow. Sub-optimal conditions, such as poor oral hygiene and high sugar diets, may exacerbate these symptoms as well. The clinical presentation of oral candidiasis as a side effect of Olanzapine integrates multiple symptoms, such as oral hygiene and the presence of diabetes, to create an environment for oral thrush to thrive. Understanding the multifactorial relationship between Olanzapine and oral candidiasis is essential in early recognition of this side effect as well as intervention, especially in vulnerable psychiatric populations.

References:

1.Patil, S., Majumdar, B., Sarode, S. C., Sarode, G. S., & Awan, K. H. (2015). Oropharyngeal candidiasis in HIV-infected patients—An update. *Frontiers in Microbiology, 6*, 1171. https://doi.org/10.3389/fmicb.2015.01171

2.Lalla, R. V., Bowen, J., Barasch, A., et al. (2014). MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer, 120*(10), 1453–1461. https://doi.org/10.1002/cncr.28592

3.Soysa, N. S., Samaranayake, L. P., & Ellepola, A. N. (2006). Diabetes mellitus as a contributory factor in oral candidosis. *Diabetic Medicine, 23*(5), 455–459.

https://doi.org/10.1111/j.1464-5491.2005.01700.x

4.Bymaster, F. P., et al. (1996). Radioreceptor binding profile of the atypical antipsychotic olanzapine. ***Neuropsychopharmacology, 14*****(2), 87–96.**

5.Dodds, M. W. J., et al. (2005). The role of saliva in maintaining oral health and preventing dental disease. ***Journal of the American Dental Association, 136*****(5), 697–706.**

6.Squier, C. A., et al. (1997). The effects of xerostomia on oral mucosa and mucosal infections. ***Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology, 83*****(5), 530–534.**

7.van Nieuw Amerongen, A., & Veerman, E. C. (2002). Saliva—the defender of the oral cavity. ***Oral Diseases, 8*****(1), 12–22.**

8.Newcomer, J. W. (2005). Second-generation (atypical) antipsychotics and metabolic effects: a comprehensive literature review. ***CNS Drugs, 19*****(s1), 1–93.**

9.Miller, B. J., Buckley, P., Seabolt, W., Mellor, A., & Kirkpatrick, B. (2011). Meta-analysis of cytokine alterations in schizophrenia: clinical status and antipsychotic effects. ***Biological Psychiatry, 70*****(7), 663–671. https://doi.org/10.1016/j.biopsych.2011.04.013**

10.Zhang, X. Y., Zhou, D. F., Zhang, P. Y., Wu, G. Y., & Su, J. M. (2004). Elevated interleukin-2, interleukin-6, and interferon-gamma levels in neuroleptic-free schizophrenia: association with psychopathology. ***Schizophrenia Research, 65*****(2–3), 109–114. https://doi.org/10.1016/S0920-9964(03)00105-0**

11.Müller, N., & Schwarz, M. J. (2010). Immune system and schizophrenia. ***Current Immunology Reviews, 6*****(3), 213–220.**

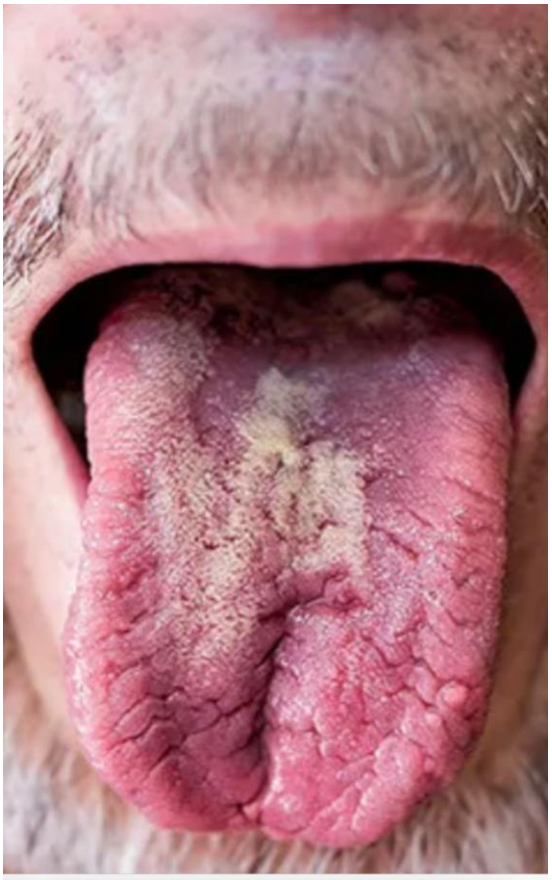


Figure 1: Case presenting with oral candidiasis