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Article type : Case Report

Title: Going through a rough patch: oral adverse effects of secukinumab

Case Report

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Abstract

Chronic hyperplastic candidiasis (CHC) clinically presents with white plaques involving the post-commissural buccal mucosa and less frequently, the tongue. Common risk factors include xerostomia, smoking, post-chemotherapy or radiotherapy, antibiotic use, vitamin deficiency and immunosuppression. Here, we present a case of CHC secondary to secukinumab.

A 38-year-old man presented with a 6-month history of asymptomatic white plaques involving the lateral tongue and buccal mucosa. The medical history included chronic plaque psoriasis controlled with secukinumab 300mg monthly, initiated 6 months prior to presentation. Intraoral examination revealed dense homogenous keratosis involving the right and left posterior lateral tongue and posterior buccal mucosa. Histopathological examination was consistent with chronic hyperplastic candidiasis. Special stains for fungal hyphae were positive. In situ hybridisation for EBV were negative. Serology was negative for HIV. He was managed with fluconazole 100mg daily for one week and placed on a prophylactic antifungal regime of chlorhexidine 0.2% mouthwash to reduce overall Candida load, however the white plaques remained unchanged. He subsequently discontinued secukinumab and switched to certolizumab, resulting in complete resolution of oral candidiasis.

In psoriasis, dysfunction in the cytokine pathway results in excessive production of IL-17A. Secukinumab, a next generation anti-IL-17A biologic, is being used more commonly to manage moderate-severe plaque psoriasis. Clinicians should be aware of the risk of development of candidiasis as a potential complication of secukinumab due to the concurrent role of IL-17 in innate and adaptive immunity against Candida. Early recognition of oral Candida lesions with diagnostic biopsy is paramount to exclude dysplasia.

**Key words:** chronic hyperplastic candidiasis; psoriasis; secukinumab

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Case report

A 38-year-old male presented with a 6-month history of asymptomatic white plaques involving the lateral tongue and buccal mucosa bilaterally. There was no change in appearance since initial detection. The medical history included chronic plaque psoriasis controlled with secukinumab 300mg monthly (initiated six months prior to his presentation). Intraoral examination revealed dense homogeneous keratosis involving the right and left posterior lateral tongue and buccal mucosa at the level of the occlusal plane (Fig. 1). Remaining soft tissues were healthy.

Histopathological examination revealed markedly hyperparakeratinised epithelium, variable hyperplasia and atrophy with elongated, rounded and broad rete pegs (Fig.2). The epithelium was acanthotic with basal cell hyperplasia. There was dense chronic inflammatory cell infiltrate within the superficial lamina propria and lymphocyte exocytosis throughout the full thickness of the epithelium. Scattered neutrophils were noted within the superficial epithelial cell layers and focal ballooning of keratinocytes. Special stains for fungal hyphae were positive (Fig.3). In situ hybridisation for Epstein-Barr virus was negative. Serology was negative for HIV.

Discussion

The patient was initially managed with fluconazole 100mg daily for one week and placed on a prophylactic antifungal regime of chlorhexidine 0.2% mouthwash to reduce overall Candida load. However, the white plaques remained unchanged. He subsequently discontinued secukinumab and switched to certolizumab, resulting in complete resolution of oral candidiasis.

CHC is caused by the commensal microbe Candida albicans and clinically presents with white plaques along the post-comissural buccal mucosa and less frequently, the tongue. Common risk factors include xerostomia, smoking, post-chemotherapy or radiotherapy, antibiotic use, vitamin deficiency and immunosuppression. It differs from other variants of candidiasis as histologically, candidal hyphae may invade into the deeper layers of the mucosa and induce epithelial atypia. The differential diagnosis for white lesions affecting the lateral borders of the tongue include oral hairy leukoplakia, lichen planus, leukoplakia and frictional keratosis.

Chronic candidiasis is associated with defects involved in Candida recognition (e.g. CARD9 and Dectin1), Th17 differentiation (e.g. STAT1 and STAT3 mutations) and IL-17 signalling (e.g. anti-IL-17 autoantibodies). In the presence of Candida, Th17 T-cells and innate lymphoid cells release IL-17 and IL-22, inducing mucosal epithelial cells to produce antimicrobial peptides which disrupt the
fungal cell membrane, leading to fungal cell death.³ Disruption of this complex network can lead to overgrowth of Candida and/or an over-exuberant immune response to Candida.

In psoriasis, dysfunction in the cytokine pathway results in excessive production of IL-17A, which is a strong inducer of inflammation contributing to tissue damage, as seen in psoriatic plaques.⁴ Having failed a number of systemic therapies for management of psoriasis, this patient developed CHC following the commencement of secukinumab, a next generation anti-IL-17A biologic, established to block the pro-inflammatory cytokine IL-17A and its downstream effects. Secukinumab has grown in popularity for the management of moderate-to-severe psoriasis due to its minimal side effect profile, rapid onset of action and efficacy at targeting difficult to treat areas.⁵

CHC lesions may regress following correction of underlying haematological deficiencies and elimination of local risk factors, including optimal denture hygiene to prevent candidal colonisation of the denture fit surface, smoking cessation and rinsing after use of corticosteroid inhaler use. Diagnosis of invasive candidiasis is often negative with an oral swab and may require a biopsy.

The mainstay of treatment includes elimination of Candida infection using a combination of intermittent systemic therapy alongside with long-term topical suppression. It has been suggested that deep-seated mucosal hyphae invasion and the production of nitrosamines by Candida may influence the malignant transformation of these oral lesions and oral cancer risk.⁶ In this case, the above management was insufficient and alternative therapies which avoid targeting the IL-17 axis were sought. The patient was switched to certolizumab, a TNF-α inhibitor also effective in the blockade of psoriatic pathogenesis, with significant improvement in oral candidiasis presentation.

Clinicians should be aware of the risk of development of candidiasis as a potential complication of secukinumab due to the concurrent role of IL-17 in innate and adaptive immunity against Candida. With the introduction of newer anti-IL-17 therapies, the potential cohort of patients at risk of oral Candida infections may rise. It is important to recognise oral signs of Candida infection and manage appropriately.

References

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Figure legend

Figure 1 Homogeneous, thick keratosis along the posterior lateral tongue. Published with the patient’s consent.

Figure 2 Hyperparakeratinised epithelium with elongated, rounded and broad rete pegs. Dense chronic inflammatory cell infiltrate within the superficial lamina propria and lymphocyte exocytosis. Haematoxylin and eosin, magnification x 5.

Figure 3 Periodic acid-Schiff stain positive for fungal hyphae. Magnification x 10.