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Case Report

A Case Report of a Successful Treatment of Ipilimumab Plus Nivolumab (IPI-NIVO)-Induced Sialadenitis with Coconut Oil

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INTRODUCTION

Ipilimumab-plus-nivolumab (IPI-NIVO) immunotherapy is increasingly used to treat various cancers, including advanced melanoma. Ipilimumab, a cytotoxic T-lymphocyte associated protein 4 inhibitor, enhances the immune response against cancer cells by allowing the primary T-cell costimulatory receptor, cluster of differentiation 28, to bind freely to cluster of differentiation 80 ligands on antigen-presenting cells.[1] Nivolumab, a monoclonal antibody, binds to programmed cell death protein 1 (PD-1), a cell-surface protein on T-cells. Normally, PD-1 binding to programmed cell death ligand 1 (PD-L1) on antigen-presenting cells prevents autoimmunity, but tumors exploit this mechanism to evade immune detection. Nivolumab inhibits PD-L1 binding to PD-1, exposing the tumor to a stronger immune response.[2]

Both medications can cause autoimmune side effects, such as rash, altered thyroid function, vitiligo, pneumonitis, hepatitis, and colitis. The rate of these adverse events increases from 27.3% for ipilimumab alone and 16.3% for nivolumab alone to 55% with combined therapy. Although adverse effects of these medications are common, immunotherapy-induced sialadenitis is rare, occurring in only 0.03-0.05% of patients on IPI-NIVO.[3]

Coconut oil has been used for oral health for centuries, notably in the practice of "oil pulling" found in ancient Ayurvedic texts.[4] Some studies suggest it reduces salivary bacterial counts, though results are mixed and often at high risk for bias.[4-6] Despite its widespread use on the Indian subcontinent, research supporting coconut oil for xerostomia and mucositis is limited.

This report discusses a metastatic melanoma patient with IPI-NIVO-induced sialadenitis complicated by xerostomia and mucositis who was successfully treated with coconut oil oral rinses.

CASE REPORT

A 59-year-old male with metastatic melanoma began treatment with IPI-NIVO soon after diagnosis. He completed four cycles of ipilimumab (3 mg/kg) plus nivolumab (1 mg/kg) every three weeks, followed by 11 cycles of nivolumab alone (3 mg/kg) every four weeks. After the ninth cycle, the patient presented with dry mouth, rawness, erythema, and pain in the oral mucosa, bilateral parotid gland swelling, and nodules near the parotid glands. He also reported extreme sensitivity to salty foods and toothbrushing, requiring dietary adjustments, but had no pain without these triggers.

These symptoms, consistent with sialadenitis complicated by xerostomia and mucositis, remained stable after the 10th cycle of immunotherapy. Both the xerostomia and mucositis were of "grade 2" severity based on the National Cancer Institute's Common Terminology Criteria for Adverse Events.[7] As he did not exhibit life-threatening symptoms like colitis or pneumonitis, corticosteroids were not initiated, and no dose reductions were made.

After the 11th cycle, the patient began using Biotene® toothpaste, which partially alleviated his dry mouth and oral mucosa rawness. Before the 12th cycle, he started using coconut oil as an oral rinse two to three times daily on his daughter's advice, which significantly relieved his symptoms. This treatment subjectively improved the flexibility, color, and moisture of his oral mucosa, reduced xerostomia, and enhanced his quality of life. The patient continued these rinses during his remaining treatments, with progressive improvement and no recurrence of symptoms. He did not require corticosteroids or dose reductions throughout the process.

DISCUSSION

While immunotherapy-induced sialadenitis was the leading suspicion in this case, there was concern that the palpable nodes might indicate progressive metastatic melanoma. To confirm the diagnosis, the patient underwent a fine needle aspiration (FNA) biopsy of his right mandibular lymph node. Pathology revealed a mixed population of benign lymphocytes, consistent with lymphoepithelial sialadenitis (Figure 1). This diagnosis is significant, as IPI-NIVO immunotherapy is known to cause sialadenitis in only 0.03% to 0.05% of patients.[3]

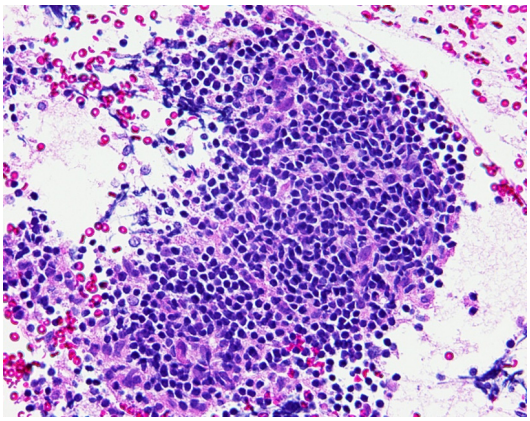

Figure 1. Mixed population of reactive lymphocytes, fine needle aspiration biopsy, 200X original magnification, hematoxylin-eosin.

Despite its rarity, sialadenitis and resultant sicca symptoms can significantly impact quality of life, making it crucial for practitioners to monitor for this side effect. While literature suggests that patients may recover with systemic or topical sialagogues such as pilocarpine,[8] systemic corticosteroids like prednisone,[9] or temporary discontinuation of immunotherapy,[10] this patient showed significant improvement using coconut oil alone.

The patient's positive response to coconut oil highlights an important consideration for providers: using nonpharmacologic therapies as first-line treatment for sicca symptoms induced by ipilimumab and nivolumab can spare patients from systemic sialagogues or corticosteroids, which have their own adverse effects. Additionally, coconut oil use may prevent delays in completing immunotherapy, which, although

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unlikely to impact treatment outcomes significantly, can cause notable distress for patients.[11]

Given the case-based nature of this report and resultant lack of any control, it is unclear whether the patient's symptoms may have improved over time without the use of coconut oil. Further, some patients may still require systemic corticosteroids, topical or systemic sialagogues, and/or delays before their next immunotherapy cycle to alleviate symptoms of sialadenitis, xerostomia, and mucositis induced by immunotherapy. However, given the case patient's significant response to coconut oil use, this therapy and/or similar oral lubricants should be considered as useful adjuncts for managing these symptoms.

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