**Dupilumab is associated with disease worsening or unmasking of Cutaneous T-cell Lymphoma**

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**Background:** Dupilumab is a biologic approved for treating moderate-to-severe atopic dermatitis (AD) with efficacy in reducing pruritus. Cutaneous T-cell lymphoma (CTCL) is an extranodal non-Hodgkin lymphoma of malignant, mature clonal T lymphocytes that infiltrate the skin. The most common subtypes of CTCL are mycosis fungoides (MF) and Sézary syndrome (SS). MF/SS and AD share similarities in clinical features including pruritus, skin impetiginization by Staphylococcus aureus, disruption of the skin barrier, and upregulation of T-helper 2 (Th2) cytokine pathways.

**Objective:** To assess the effects of dupilumab on the disease course of patients diagnosed with CTCL.

**Method:** Retrospective chart review of 7 patients who were treated with dupilumab and either diagnosed with CTCL following initial diagnosis of AD, or experienced rapid progression of previously diagnosed CTCL.

**Results:** Seven patients (3 female; median age=65.5 years [range 40-77]) who received dupilumab were identified. Dupilumab was initiated for clinically presumed AD in four patients and used off-label in CTCL (stages IB-IIIB) with pruritus in three patients (median duration=4 months [range 3-27]). Six of seven experienced initial improvement (median duration=2 months [range 1-8]), followed by worsening body surface area (n=7), pruritus (n=5), lymphadenopathy (n=3), and systemic symptoms (n=3). The four patients with clinically presumed AD were diagnosed with CTCL/MF. The three patients with existing CTCL prior to dupilumab developed worsened blood involvement on flow cytometry and were diagnosed with Sézary syndrome while on treatment. Two of the three died of disease progression.
Conclusion: The purpose of this case series is to increase awareness of similarities between AD and CTCL, and caution providers against using dupilumab for CTCL patients. Although dupilumab may relieve pruritus and temporarily reduce body surface area burden, it may then lead to rapid progression of disease. Therefore, if clinicopathologic features for AD are atypical and MF remains a possibility, we encourage pathologists to seek a second consensus opinion before signing out the case. Furthermore, our observations highlight the need for caution when using dupilumab in patients with atypical dermatitis presentations without prior exclusion of CTCL via skin biopsy, testing for TCR gene rearrangement, and flow cytometry of the blood. Warning signs suggestive of CTCL for patients with presumed atopic dermatitis while on dupilumab therapy include new eczematous plaques in locations different than original sites, worsening pruritus, lymphadenopathy and new onset moderate-severe “atopic dermatitis” in the elderly. As dupilumab becomes more commonplace in the treatment of AD and atopic disease, we anticipate seeing a greater number of cases of unmasked CTCL in patients initially diagnosed with AD.

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