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Title

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Journal

Dermatology Online Journal, 29(1)

Authors

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Publication Date

2023

DOI

10.5070/D329160224

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Peer reviewed

JAK inhibitors for dermatitis herpetiformis: check the gut!

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Keywords: celiac disease, dermatitis herpetiformis, JAK inhibitor, lymphoma

To the Editor:

We read with great interest the recent case report published in *Dermatology Online Journal* about the successful use of tofacitinib, a Janus kinase (JAK) inhibitor, in managing a refractory dermatitis herpetiformis [1]. However, we would emphasize the necessity to check for any associated refractory celiac disease (RCD) or even a hidden enteropathy-associated T-cell-lymphoma (EATL) in such patients before starting any JAK inhibition therapy. In fact, some celiac patients are prone to develop RCD, notably RCD type-2 (RCD2), a clonal lymphoproliferation emerging from innate intraepithelial lymphocytes [2]. This RCD2 is associated with an increased risk of the so-called enteropathy-associated T-cell lymphoma (EATL) and thus considered as a pre-lymphoma stage [3]. Its diagnosis relies on a panel of gastrointestinal investigations (endoscopy, imaging, and pathology techniques such as immunohistochemistry and even flow cytometry), [2].

Interestingly, among the several genetic risk factors for RCD that were recognized, JAK1 and STAT3 mutations were identified in abnormal intraepithelial cells in patients with RCD2 [4]. In addition to RCD2, the other risk factors for EATL are older age,

male gender, presence of ulcerative jejunitis, and presence of aberrant T cells [5,6].

Thus, upper digestive endoscopy with intestinal biopsies are recommended to look for any predisposing or established malignant lesions (i.e., RCD and EATL) before and during such immunotherapy. This is particularly important in elderly, male patients—as in this case report—who are considered at high-risk for such complications and do require careful monitoring.

Of note, lymphoma and other malignant tumors were reported in clinical studies of patients treated with the JAK inhibitor tofacitinib, and the Food and Drug Administration recommends weighing the benefits and risks when considering tofacitinib in patients who develop malignancies [7]. We recommend thorough screening and longitudinal monitoring of CD patients (via endoscopy and frequent celiac serologies) when initiating such JAK inhibition to prevent a delay in diagnosis of severe complications like RCD.

Potential conflicts of interest

The authors declare no conflicts of interest.

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