12-2020

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Recommended Citation

Vellaichamy G, Townsend SM, Lyons AB, and Hamzavi IH. T-cell/histiocyte-rich large B-cell lymphoma in a 27-year-old with hidradenitis suppurativa, psoriasis, and vitiligo: Implications for screening. JAAD Case Reports 2020; 6(12):1252-1253.

T-cell/histiocyte-rich large B-cell lymphoma in a 27-year-old with hidradenitis suppurativa, psoriasis, and vitiligo: Implications for screening

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Key words: hidradenitis suppurativa; lymphoma; psoriasis; vitiligo.

INTRODUCTION

Hidradenitis suppurativa (HS), psoriasis, and vitiligo are chronic, immune-mediated skin diseases with a significant quality-of-life burden. Individuals with these conditions are thought to be at increased risk of lymphoma,[1-3] and several cases have been reported in the context of adalimumab treatment, raising concern for its use in at-risk patients. The specific mechanisms underlying the link between chronic inflammatory states and neoplastic transformation are largely unknown, and most data on the topic come from cases outside of dermatology (ie, rheumatoid arthritis, ulcerative colitis).[4] We present the unusual case of a patient with HS, psoriasis, and vitiligo on long-standing treatment with adalimumab who went on to have T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) and evaluate the factors that led to this pathologic condition.

Abbreviations used:

HS:	hidradenitis suppurativa
THRLBCL:	T-cell/histiocyte-rich large B-cell lymphoma

CASE PRESENTATION

A black woman had chronic plaque psoriasis without psoriatic arthritis beginning at age 5 and generalized vitiligo at age 18. Topical treatments were trialed but had minimal effect on either disease, and initial treatment with apremilast was ineffective. Adalimumab was initiated at age 23 every 2 weeks for psoriasis, which proved to be effective. Months later, she began to develop abscesses and nodules in the axillae, inframammary region, and groin, which continued to flare with greater intensity. At age 25, HS was diagnosed (Hurley stage III in axillae, stage II in groin), and adalimumab dosing was increased to weekly for her HS but showed minimal efficacy. No family history of HS, psoriasis, or vitiligo was noted. At age 26, during an admission for an HS flare, she had an unexplained fever, inguinal lymphadenopathy, and mild nausea, vomiting, and abdominal pain. Elevated liver enzymes were found, and further imaging found multiple liver lesions and enlarged retroperitoneal and inguinal lymph nodes. Lymph node biopsy found THRLBCL. Adalimumab was stopped, and chemotherapy was initiated with complete response for her lymphoma. Liver function tests were monitored at biweekly intervals for 6 months followed by once every 3 months and normalized 1 month after treatment initiation. Her psoriasis did not return, but her HS and vitiligo continue to require medical management.

DISCUSSION

THRLBCL development following adalimumab administration was reported once before in a case of severe psoriasis resistant to other immunosuppressive regimens.[5] Although similar reports exist, the cumulative evidence to date has shown little to no effect of adalimumab treatment on lymphoma development, THRLBCL or otherwise.[4,6,7] Conversely, HS (2- to 4-fold increase), psoriasis (1.4-fold increase), and

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Funding sources: None.

Conflicts of interest: Dr Lyons is a subinvestigator for Incyte, Pfizer, Lenicura, and General Electric. Dr Hamzavi is President of the Hidradenitis Suppurativa Foundation (unpaid), Co-Chair of the Global Vitiligo Foundation (unpaid), member of the Abbvie Advisory Board (unpaid), a consultant for Incyte, and an investigator for Incyte, Pfizer, PCORI, General Electric, and Lenicura. The rest of the authors have no conflicts to disclose.

IRB approval: This study is IRB exempt.

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JAAD Case Reports 2020;6:1252-3.
2352-5126

https://doi.org/10.1016/j.jdcr.2020.08.032

vitiligo (3-fold increase) are each independently associated with increased lifetime risk of lymphoma.[1-3] Although the specific mechanisms remain elusive, this observation is postulated to be the result of chronic lymphocyte activation that increases the probability of a monoclonal subset arising.[3] Interestingly, risk of lymphoma development in rheumatoid arthritis patients increases with increasing inflammatory disease activity; patients with low and medium inflammatory activity exhibited up to an approximately 8-fold (odds ratio, 7.7 [95% confidence interval, 4.8-12.3]) increased risk, but those with high activity demonstrated up to approximately 71-fold (odds ratio, 71.3 [95% confidence interval, 24.1-211.4]).[7] This finding is compelling, as it suggests that although most patients will not observe a clinically significant lymphoma risk within their lifetime, those with high inflammatory burdens, such as our patient with long-standing, severe psoriasis and HS, may experience extremely high odds of lymphoma development. Such dermatology patients may benefit from screening for lymphoproliferative disease, if only through a brief assessment of clinical symptoms such as lymphadenopathy, unexplained fever, night sweats, or weight loss.[8]

THRLBCL is a rare, aggressive variant of non-Hodgkin lymphoma that is histologically characterized by few neoplastic B-cells within a stroma of mostly histiocytes and T cells, primarily $CD4^+$.[9] Gene expression studies highlight an interferon-γ—dominant signature that differentiates this lymphoma subtype from the more common Hodgkin disease,[9] which may drive the recruitment of the reactive phagocytes to the stroma. Assessment of subtype-specific relative risks show that specific inflammatory diseases associate highly with certain non-Hodgkin lymphoma subtypes but not others,[4] suggesting that underlying disease-specific pathways may exist that explain these connections. To this regard, vitiligo is well known to be driven by excessive interferon-γ signaling and may have played a role in propagating this unique histologic variant,[10] but little direct evidence exists to date. HS and psoriasis share overactivity of the interleukin-23/T-helper cell 17/interleukin-17 immune axis, but the relevance of that pathway in this context is unclear.

We present the case of a young woman with HS, psoriasis, and vitiligo being treated with adalimumab that presented with an aggressive variant of lymphoma. Our investigation suggests that this patient's high inflammatory burden was the most significant driver of this condition, which brings up implications for screening in select at-risk dermatology patients. Further reports and direct evidence, particularly from studies of inflammatory skin disease, may help to elucidate the mechanisms underlying these observations.

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