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Hidradenocarcinoma in a Crohn's patient on ustekinumab: A case report

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Abstract

Hidradenocarcinoma is a locally aggressive malignancy of the sweat glands, most commonly found on the head, neck, and upper body. Although rare, it has been seen in patients with hidradenitis supparativa, who have an increased risk of non-melanoma skin cancers. Ustekinumab, a biologic agent used to treat inflammatory bowel disease, has been associated with development of cancer in some patients. We present a case of a 36-year-old female with hidradenitis supparativa and Crohn's disease who developed hidradenocarcinoma in setting of ustekinumab use, demonstrating the need for further study of the relationship between biologic therapy and malignancy.

Keywords

Hidradenitis supparativa, hidradenocarcinoma, Crohn's disease, ustekinumab, case report

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Introduction

Hidradenocarcinoma, a rare and aggressive tumor arising from the intradermal duct of the eccrine sweat glands,[1] has no clear risk factors except for the presence of hidradenoma, though more typically the malignancy arises de novo while hidradenoma more frequently predisposes to squamous cell carcinoma.[2] More generally speaking, risk factors for eccrine tumors can include a family history, as well as smoking and obesity, and lesions are likelier to arise with older age.[2] The tumor typically presents as a solitary, subcutaneous mass, arising most commonly in the head and neck, with high risk of metastasis and recurrence, often resulting in poor prognosis. Diagnosis can be challenging given nonspecific clinical presentations, and potentially slow initial growth, thus requiring high index of suspicion.[1,2] Treatment is highly varied due to the rarity of the condition, though local excision with wide margins is a mainstay and radiation is frequently employed.[2,3] Adjuvant chemotherapy with some combination of platins, bleomycin, cyclophosphamide, doxorubicin, and/or trastuzumab may also be employed.[2] Biologic therapies are increasingly used in the management of hidradenitis supparativa (HS),[4] and have been used in Crohn's disease (CD) for some time. However, these therapies have been associated with several non-eccrine skin cancers,[5] but the rarity of hidradenocarcinoma makes it more difficult to study associations in the context of a single or even multicenter study. Here we present the case of a 36-year-old woman with a history of HS, CD, and multiple adverse events to biologic therapy, who developed hidradenocarcinoma in the context of ustekinumab therapy.

Case report

A 36-year-old white woman former smoker (2-pack-year) on ustekinumab (initiated in 2020) with a history of HS, inflammatory ileal CD, type 2 diabetes mellitus, and adverse events in response to adalimumab (initiated in 2012, discontinued in 2013 due to drug induced lupus), infliximab (initiated in 2011,

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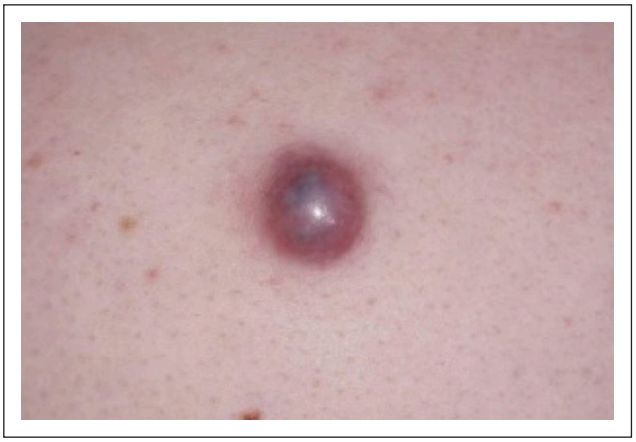

Figure 1. An image of the tumor located on the patient's back.

discontinued in 2012 due to joint pain), and vedolizumab (initiated and discontinued in 2017 due to bacteremia), presented with a solitary $6 \times 2.5\,cm^2$ mass on her back (Figure 1) in February of 2022. The mass had been present for several years. The patient experienced an onset of soreness, itching, and erythema surrounding the lesion which worsened after attempts to manually express it, and finally sought medical attention when she experienced worsening pain and pruritus. Her maternal grandfather had skin cancer of unclear type, but she has no other family history or personal history of skin malignancy. The nodule was superficially biopsied and epithelial cells stained positive for EP-CAM, variably positive for MCK, CK7, CK20, and CEA, and basal cells stained positive for p63. Synaptophysin and adipophilin staining was negative. The lesion was diagnosed as an atypical cutaneous adnexal tumor, consistent with low-grade hidradenocarcinoma. Computed tomography imaging confirmed no metastasis had occurred. Ustekinumab was discontinued, and the patient underwent local excision of the tumor with 2 cm margins with sentinel nodal mapping. The lesion was excised at the level of the fascia, which included all subcutaneous fat, resulting in removal of $8 \times 4\,cm^2$ of tissue. All margins and sentinel nodes were benign. She elected to not receive radiation therapy but will undergo surveillance exams every 6 months.

Discussion

Hidradenocarcinoma is a rare and locally aggressive malignancy of the sweat glands that frequently metastasizes and is associated with a high rate of recurrence.[3] It is referred to by multiple names in the literature, and sometimes is categorized into apocrine and eccrine subtypes, despite the fact that these categories may not have differential identifying staining or disease prognosis.[6] Hidradenocarcinoma makes up less than 0.01% of all skin cancers and rarely results from a pre-existing hidradenoma, as it typically arises de novo.[7] Most commonly found on the head, neck, and upper body,[2] hidradenocarcinoma typically presents as a well-circumscribed, solitary, subcutaneous, firm nodule, sometimes with telangiectasia and/or ulceration. Most patients are asymptomatic; however, they may present with pain, ulceration, or bleeding of the tumor with physical contact.[7] With time, the tumor may spread regionally, usually to the lymph nodes or metastatically, with some patients remaining asymptomatic even after metastatic spread of the disease.[8] The diagnosis of hidradenocarcinoma is confirmed with a panel of immunohistochemical stains for p53 or p63, keratins, and cytokeratins, but specific stains are inconsistent, as are treatment guidelines.[7] Wide surgical excision is the mainstay of treatment, and early diagnosis critical; however, postsurgical recurrence rates have been found to be as high as 50%. Both radiotherapy and chemotherapy have both been used in the treatment of this malignancy, but their efficacy remains uncertain, creating a lack of consensus on current treatment guidelines.[8]

While hidradenocarcinoma is itself rare, skin cancer in patients with HS is not.[9] Patients with HS are at 2-fold increased risk of non-melanomatous skin cancers (NMSC). Similarly, patients with inflammatory bowel disease (IBD) are at increased risk of developing NMSC, independent of immunosuppressant use.[10] Therefore, patients with both HS and IBD are likely at an even higher risk of developing these malignancies. Biologic therapies are increasingly used to manage both diseases;[4] however, the relationship between newer biologic therapies and the development of malignancy is unclear. Anti-TNFs have been associated with an increased risk of cancer, mainly melanoma, lymphoma, and NMSCs,[5,11] but studies in non-US populations have not consistently validated those findings.[12] Additionally, recent research has reported no difference in skin cancer recurrence while on biologic therapy, including ustekinumab[13]; however, the lack of longitudinal large cohort studies makes it difficult to establish a clear relationship. Similarly to anti-TNF medications, anti-IL12/23 (ustekinumab) exposure has been associated with rapid progression or onset of cancer in multiple case reports, particularly of aggressive cancers.[14,15] It has been hypothesized that immunosuppression allows for subclinical malignancy to progress,[16] which would align with observations in our patient. To our knowledge, this is the first report of a patient with CD and HS developing hidradenocarcinoma in the context of ustekinumab exposure. Given the aggressive nature of hidradenocarcinoma, early diagnosis and treatment are crucial. As such, clinicians need to have a high index of suspicion for this diagnosis when similar skin lesions are detected.

Conclusion

To our knowledge, this case of a 36-year-old female on ustekinumab with a history of HS and inflammatory ileal CD who developed hidradenocarcinoma is the first to be reported. Given the inconclusive evidence to date on the risk of

malignancy in patients treated with biologic therapy, this case highlights the importance of further investigation into possible associations between rarer dermatologic malignancies and biologic therapy. This is especially necessary in patients with IBD who have an increased risk of malignancy at baseline and are often treated with these biologic agents. Additionally, given the aggressive nature of certain malignancies like hidradenocarcinoma, physicians must be aware of these possible associations and have a high index of suspicion when skin lesions and other signs of malignancy are detected.

Author contributions

M.A. reviewed the literature and wrote and revised the manuscript. E.Z. and U.W. wrote and revised the manuscript. All authors approved the final manuscript. U.W. is the article guarantor.

Declaration of conflicting interests

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Ethics approval

Ethical approval is not required for this study in accordance with local or national guidelines.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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