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Squamous cell carcinoma of the cervix arising in a patient on adalimumab – a need for cervical screenings in patients on tumor necrosis factor inhibitors

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Abstract

Adalimumab, a tumor necrosis factor (TNF) inhibitor, has been approved for treatment of hidradenitis suppurativa. We report a case of cervical cancer in a patient with hidradenitis suppurativa taking adalimumab, which prompted discontinuation of the medication. Physicians should obtain a detailed cervical medical history before putting a female patient on a TNF inhibitor. Patients on TNF inhibitors who have pre-existing cervical issues such as human papillomavirus (HPV), dysplasia, or high grade intraepithelial lesions should be counseled about an increased risk of developing squamous cell carcinoma (SCC) of the cervix while on a TNF inhibitor. Furthermore, patients on TNF inhibitors should comply with the national screening guidelines for cervical cancer and be tested for human papillomavirus.

Keywords: adalimumab, cervical cancer, squamous cell carcinoma, human papillomavirus, hidradenitis suppurativa, tumor necrosis factor inhibitor

Case Synopsis

We present a 33-year-old woman with stage III hidradenitis suppurativa who began treatment with adalimumab, a TNF inhibitor, at a preliminary dose of 40 mg per week. Over the course of 6 months patient showed minimal improvement and the dose was increased to 80mg/week, as appropriate for the patient's BMI (50.7 kg/m2), [1], with good response. The patient indicated that she had no prior history of SCC. However, her history of high-risk HPV, high grade squamous intraepithelial lesion (HGSIL), and mild dysplasia (CIN I) of the endocervix that was confirmed by immunohistochemistry was not disclosed. These lesions had resolved with treatment, as indicated by a negative pathology examination a year before starting adalimumab. At the end of the 8th month on adalimumab the patient was diagnosed with a new cervical lesion. Curettage of the endocervix showed a HGSIL and pathology revealed severe dysplasia/squamous cell carcinoma (SCC) in situ (CIN III) with focal endocervical gland involvement. The fact that the patient developed cervical SCC, which if left untreated can develop into metastatic SCC [2], necessitated discontinuation of adalimumab.

Case Discussion

There has been evidence linking TNF inhibitors to cervical dysplasia and cancer. A recent study showed that women with rheumatoid arthritis (RA) taking a TNF inhibitor are at increased risk of CIN II-III and invasive cervical cancer when compared to RA patients who were biologics-naive [3]. Furthermore,

another study concluded that women with inflammatory bowel disease who underwent exposure to an immunosuppressant agent, including infliximab, had a higher risk of an abnormal Pap test associated with HPV than unexposed patients [4]. Human papillomavirus reactivation from the latent state has been noted in immunocompromised patients and the use of immunosuppressive agents such as TNF inhibitors can possibly increase the risk of persistent HPV infection and ultimately cervical cancer [5]. Along the same lines, there are reports of perianal condylomata associated with etanercept treatment in a woman with history of condylomata and exacerbation in pre-existing genital HPV lesions in a patient on infliximab [6]. Furthermore, HPV has been detected in SCC of immunosuppressed patients [7]. Furthermore, an HPV-positive woman developed metastatic rectal SCC after taking etanercept [8].

Conclusion

We propose that patients started on TNF inhibitors be made aware that they have an increased risk of developing SCC of the cervix if they have preexisting cervical conditions such as HPV identification, dysplasia, or high grade intraepithelial lesions. It has been recommended to exercise caution when prescribing TNF inhibitors to patients with premalignant conditions like cervical dysplasia [9]. Patients taking TNF inhibitors should comply with the national screening guidelines for cervical cancer and be tested for HPV [10]. A consensus paper about current screening guidelines for cervical cancer suggests that increasing access to screening among women who are currently unscreened or screened infrequently can lead to the greatest reduction of cervical cancer incidence and mortality [10]. Patients' HPV records and vaccinations as well as all cervical screening results should be disclosed to their prescribing health care professional before being started on a TNF inhibitor. Furthermore, it is necessary to discontinue adalimumab if cervical cancer develops.

References

1. Rosas J, Llinares-Tello F, Senabre-Gallego JM, Barber-Vallés X, Santos-Soler G, Salas-Heredia E, et al. Obesity decreases clinical efficacy and levels of adalimumab in patients with ankylosing spondylitis. *Clin Exp Rheumatol.* 2017,35(1):145-148. [PMID: 27908311].
2. Giesey R, Delost GR, Honaker J, Korman NJ. Metastatic squamous cell carcinoma in a patient treated with adalimumab for hidradenitis suppurativa. *JAAD Case Reports.* 2017,3(6):489-491. [PMID: 29022006].
3. Wadström H, Frisell T, Sparén P, Askling J. Do RA or TNF inhibitors increase the risk of cervical neoplasia or of recurrence of previous neoplasia? A nationwide study from Sweden. *Ann Rheum Dis.* 2016,75(7):1272-8. [PMID: 26755797].
4. Kane S, Khatibi B, Reddy D. Higher incidence of abnormal Pap smears in women with inflammatory bowel disease. *Am J Gastroenterol.* 2008,103(3):631-6. [PMID: 17941962].
5. Kim SY, Solomon DH. Tumor necrosis factor blockade and the risk of viral infection. *Nat Rev Rheumatol.* 2010,6(3):165-74. [PMID: 20142812].
6. Antoniou C, Kosmadaki MG, Stratigos AJ, Katsambas AD. Genital HPV lesions and molluscum contagiosum occurring in patients receiving anti-TNF- therapy. *Dermatology.* 2008,216(4):364-5. [PMID: 18285688].
7. Rust A, McGovern RM, Gostout BS, Persing DH, Pittelkow MR. Human papillomavirus in cutaneous squamous cell carcinoma and cervix of a patient with psoriasis and extensive ultraviolet radiation exposure. *J Am Acad Dermatol.* 2001,44(4):681-6. [PMID: 11260548].
8. Silverton A, Raad RA, Katz L, Downey A, Muggia FM. Squamous cell carcinoma of the rectum: a consequence of immunosuppression resulting from inhibiting tumor necrosis factor (TNF)? *Ecancermedicalscience.* 2016,10:646. [PMID: 27350791].
9. Raval G, Mehta P. TNF-α inhibitors: are they carcinogenic? *Drug Healthc Patient Saf.* 2010,2:241-7. [PMID: 21701636].
10. Saslow D, Solomon D, Lawson HW, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for the Prevention and Early Detection of Cervical Cancer. *CA Cancer J Clin.* 2012,62(3):147-72. [PMID: 22422631].