Received: 29 December 2021 | Revised: 1 April 2022 | Accepted: 5 April 2022

DOI: 10.1111/dth.15503

DERMATOLOGIC THERAPY WILEY

LETTER

Cutaneous tuberculosis induced by adalimumab

Dear Editor,

Adalimumab (Humira®, AbbVie Inc., North Chicago, IL, USA) is a fully human monoclonal antibody specific for tumor necrosis factor-α (TNF-α) that is approved for the treatment of moderate-to-severe hidradenitis suppurativa who did not respond to classical systemic treatment.[1] Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease that is characterized by recurrent painful nodules, abscesses and draining sinus tracts mainly in intertriginous areas. It could cause severe impact on patients' quality of life.[2] Patients treated with TNF-α antagonists are at increased risk for tuberculosis during treatment. And if that occurs they usually present with disseminated or extrapulmonary disease.[3]

A 26-year-old female patient presented with a painless lesion on the lateral aspect of right hand third nail that did not heal for about 8 weeks. There was no history of trauma, but she came from rural area. There was no weight loss, fatigue, cough, and night sweats. She did not benefit from topical and systemic antibiotic treatments. It was learned from her history that she had used 40 mg/week sc adalimumab for about 2 years due to resistant hidradenitis suppurativa. It is not known whether or not the patient was investigated for tuberculosis infection before the adalimumab treatment. When the patient was evaluated with the Autoinflammatory Disease Damage Index (ADDI), which has recently been used in the evaluation of HS patients, only musculoskeletal pain was present, while other items were absent.[4]

Dermatological examination revealed a painless erythematous, edematous, hemorrhagic crusted plaque with a verrucous surface around the nail plate, distal to the third finger of the right hand (Figure 1). There was no significant finding in her laboratory examinations except for mild C-reactive protein (CRP) elevation. Incisional biopsy revealed papillomatosis and acanthosis in the epidermis, granulomatous structures in the dermo-epidermal junction and upper dermis. Granulomas consisted of epithelioid histiocytes and Langhans-type giant cells and tended to colalescence. Lastly, there were large foci of caseification necrosis (Figure 2). There was no growth in tissue culture.

Adalimumab-induced cutaneous tuberculosis diagnosed with clinical and histopathological findings. Adalimumab treatment discontinued. She was evaluated in terms of underlying pulmonary tuberculosis. The patient's purified protein derivative (ppd) test result was 10 mm. Thorax computed tomography was taken and no evidence of active or latent tuberculosis was detected. The patient was started to quadruple (rifampicin, isoniazid, pyrazinamide and ethambutol) tuberculosis treatment. At her sixth month follow-up, the lesion completely regressed (Figure 3). She did not experience any exacerbation of HS during the follow-ups.

TNF-α antagonists are increasingly used in the treatment of a wide variety of inflammatory diseases, such as rheumatoid arthritis, ankylosing spondylitis, psoriasis, psoriatic arthritis, inflammatory bowel diseases and HS. Increasing use of TNF-α antagonists also increases the incidence of new tuberculosis infections or reactivation of latent tuberculosis.[5] Tuberculosis is an infectious disease caused by acid-fast bacilli belonging to the Mycobacterium tuberculosis complex that can affect lungs and other organs. Extrapulmonary tuberculosis is rare and accounts for only about 15% of all tuberculosis cases.[6] Cutaneous tuberculosis, in particular constitutes only 0.5%–2% of all extrapulmonary tuberculosis cases and is very rare.[7] As far as we know, cutaneous tuberculosis related to the adalimumab use has not

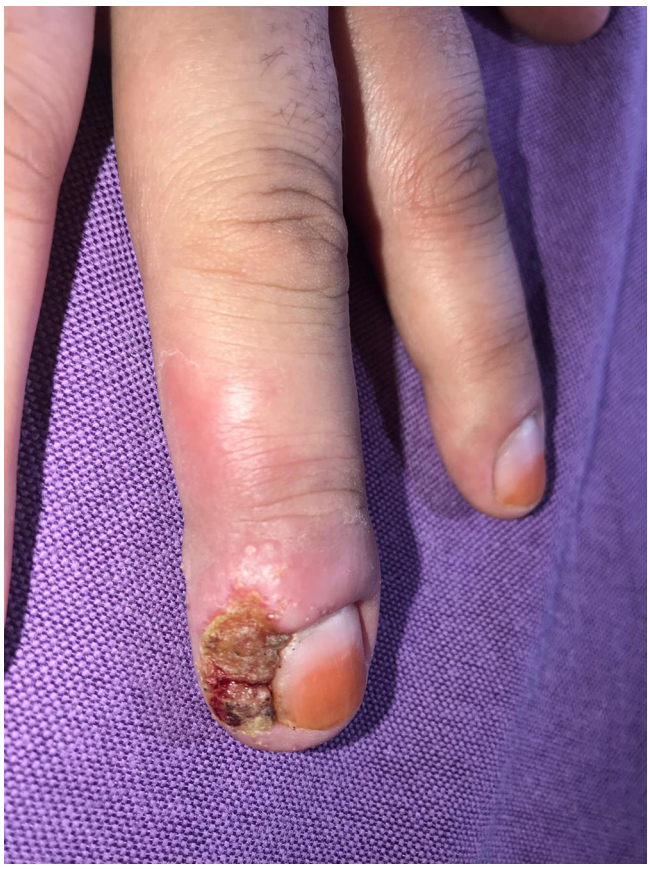

FIGURE 1 Painless erythematous, edematous, hemorrhagic crusted plaque with a verrucous surface around the nail plate

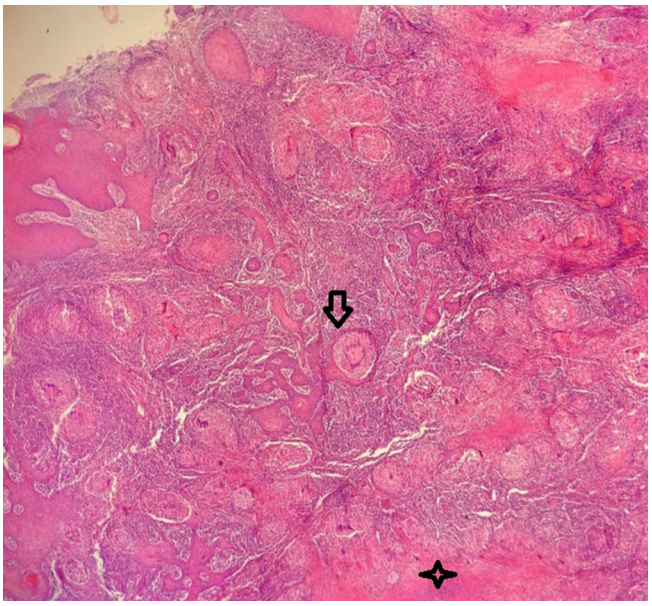

FIGURE 2 There is papillomatous and acanthosis in the epidermis and granuloma structures (arrow) are observed in the upper dermis that attach to epidermis. Granulomes tend to coalesce and contain caseification necrosis (asterix) (HEX100)

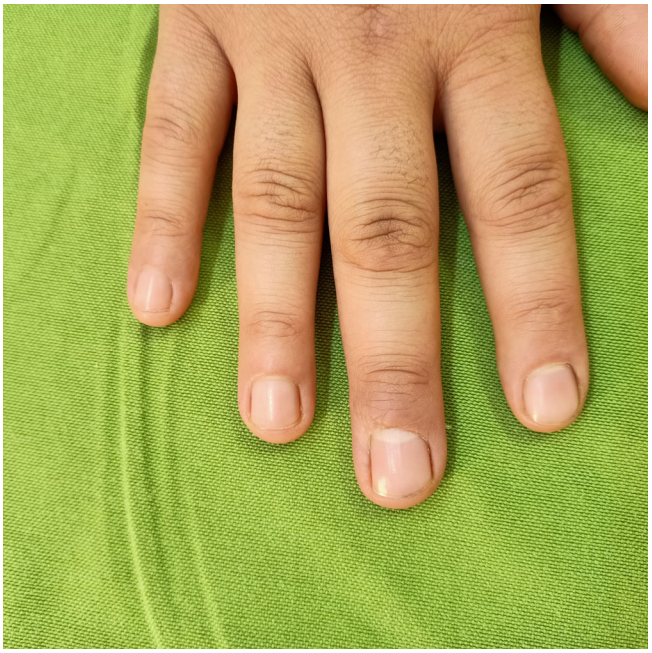

FIGURE 3 Appearance of lesions after treatment

been reported in the literature before. Therefore, we found it appropriate to present this case because of its very rare occurrence.

Cutaneous tuberculosis may present with many different clinical manifestations and may mimic many diseases. It could develop exogenously with a primary lesion as seen in tuberculosis verrucosa cutis and tuberculous chancre. Tuberculides may also occur secondary to the spread of systemic disease as in the form of lupus vulgaris, acute cutaneous miliary tuberculosis, or orificial tuberculosis.[8] In this case, the patient came from a rural area and the lesion developed on the finger. Therefore, we concluded that the patient was sensitized by this bacillus before, infected exogenously. The use of adalimumab played a role in facilitating the infection. The fact that the patient did not have a suspicious focus in her lung and the absence of constitutional symptoms accompanying the lesions also supported our hypothesis.

In the literature, there is very little data regarding the development of extrapulmonary tuberculosis in patients receiving TNF-a therapy. Ferreira et al. reported tuberculous tonsillitis in a patient who used adalimumab for Behçet's disease. The authors stated that tuberculosis should definitely be kept in mind in patients who use TNF-α antagonists in cases mimicking throat infection and even malignancies resistant to the conventional treatments.[9] Similarly, Derk et al. reported tuberculous tonsillitis in a case using etanercept for rheumatoid arthritis.[10] In addition, a patient with ankylosing spondylitis treated with infliximab and diagnosed with splenic tuberculosis was reported.[6]

When a cutaneous tuberculosis infection is suspected based on the patient's history, risk factors, and physical examination, the available diagnostic tests are ppd, histopathological examination, culture, and polymerase chain reaction (PCR).[11] In this case, the history of adalimumab use, ppd positivity, and typical histopathological findings including caseification necrosis made us to diagnose cutaneous tuberculosis. There was also an excellent response to antituberculosis therapy. Once diagnosed, the approach is similar to the treatment of pulmonary tuberculosis. According to the Centers for Disease Control and Prevention, the standard regimen is a two-month course of rifampicin, isoniazid, pyrazinamide, and ethambutol followed by 4 months of rifampicin and isoniazid only. Surgical excision, cryotherapy, and electrocautery may be used in addition to the medical treatment.[12]

In conclusion, dermatologists should keep cutaneous tuberculosis in mind with the differential diagnosis of an unusual, chronic, non-healing lesion that could not be explained otherwise. It should be noted that patients treated with TNF-α antagonists are predisposed to tuberculosis infection. Careful evaluation at the beginning of the treatment and long-term follow-up of patients taking such drugs are still required.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Gülhan Gürel: Conceptualization, data curation, formal analysis, methodology, resources, writing-original draft, writing-review and editing. Çiğdem Özdemir: Conceptualization, writing-review and editing, supervision. İrem Nur Durusu: Methodology, resources, data curation, supervision.

ETHICS STATEMENT

Written consent of the patient was obtained.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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