A Case of Erythema Induratum Case Presenting with Non-Healing Diabetic Foot Ulcer

İyileşmeyen Diyabetik Ayak Yarasıyla Başvuran Eritema İnduratum Olgusu

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Abstract
Erythema induratum of Bazin is known as a hypersensitivity response due to Mycobacterium tuberculosis. Generally, it is diagnosed by a negative skin biopsy, negative culture of Mycobacterium tuberculosis and by regression of the lesions after anti-tuberculosis therapy. We present this case to shed light on this rarely observed condition during which lesions may regress via anti-tuberculosis therapy and to point out that tuberculosis therapy should be considered for cases with non-healing diabetic foot ulcer.

Keywords: Diabetic foot ulcer, tuberculosis, erythema induratum

Introduction
Mycobacterium tuberculosis can cause disease by settling in any tissue or organ. While it often involves the lungs and the pleura, it can also present as extrapulmonary tuberculosis. The comorbidity rate of extrapulmonary tuberculosis with pulmonary tuberculosis is reported to be 60% (1). Tuberculous lymphadenitis is the most common form of extrapulmonary tuberculosis. Cutaneous tuberculosis is generally caused by M. tuberculosis, and rarely by non-tuberculous mycobacteria and atypical mycobacteria. Skin lesions occurring due to tuberculosis-related hypersensitivity reaction include erythema induratum (EI) and papulonecrotic tuberculid.

EI was first defined by Bazin in 1861 (2). It has two types: EI of Bazin type, which is associated with tuberculosis infection, and nodular vasculitis type that is not associated with tuberculosis (3). EI of Bazin type is known as a hypersensitivity response due to Mycobacterium tuberculosis. While these patients usually do not have any chest x-ray findings suggesting pulmonary tuberculosis, they have strong positivity in their purified protein derivative (ppd) readings (4). In their case, their condition is not usually accompanied by systemic symptoms such as fever, weight loss, and night sweats associated with tuberculosis infections.

Case Report
A 69-year-old female patient, who had been followed for diabetes mellitus (DM) for the past 20 years, was hospitalized in the endocrinology department at Erciyes University for DM regulation. The department of infectious diseases was consulted as the patient had nodular lesions, which were necrotic in the middle and had discharge, on her lower extremity. The non-specific
culture obtained from the discharge did not show any growth. Antibiotherapy was started and debridement was recommended after the patient did not respond to non-specific antibiotic therapy. The patient was evaluated in the pulmonary diseases department as the lesions progressed despite the repeated debridement procedures and the patient had a positive tuberculin skin test. The physical examination results were as follows: no fever at follow-ups, blood pressure of 130/70 mmHg, pulse 100/min, respiratory rate of 14/min, tachycardia, and nodular lesions that were necrotic in the middle with discharge (Figure 1, 2). Other systemic examinations were normal. The laboratory findings included hemoglobin A1c (HbA1c): 7.8%, C-reactive protein: 21.9 mg/L, sedimentation: 36 mm/sec, white blood cell count: 5800/μL, and hemoglobin (Hgb): 12.3 g/ dL; while other biochemical parameters were normal. The posteroanterior lung X-ray displayed suspicious calcified left hilar nodules (Figure 3). Computed tomography of the thorax displayed calcified parenchymal granulomas in the left upper lobe and the left hilus (Figure 4, 5). Bronchoscopy was performed since the patient could not provide phlegm, however, it was non-diagnostic. The bronchoalveolar lavage was negative for acid-resistant bacilli (ARB). A skin biopsy was recommended due to the persistent skin lesions, in order to study the tissue ARB and the culture. Skin tissue ARB was negative, and the pathology results indicated the diagnosis of El of Bazin type. Cause of lower extremities lesions such as cutaneous para-aortic lymph nodes, subcutaneous sarcoidosis, and cutaneous T-cell lymphoma were excluded by biopsy. The patient was started on 4-drug anti-tuberculosis treatment (isoniazid, pyrazinamide, rifampicin, ethambutol) and her lesions were observed to regress after two weeks. BACTEC and Löwenstein-Jensen culture growth was not detected in the bronchoalveolar lavage or the skin tissue. We

Figure 1, 2. Ulcerated nodular lesions in the lower extremity

Figure 3. Left hilar calcified appearance

Figure 4. A calcified intraparenchymal nodule in the left upper lobe

Figure 5. Left hilar calcification
aimed to report this case as it is a rarely observed condition and to emphasize that tuberculosis infection should always be considered in case of diseases that impair immunity such as DM.

Discussion

Diabetic foot ulcer is one of the most important complications of diabetes following the course of ulceration, infection and gangrene and requires inpatient treatment at hospital (10). About 56% of diabetic foot ulcers are accompanied by an infection (11). Aerobic gram-positive cocci and particularly Staphylococcus aureus are the most common agents in diabetic foot ulcer. Gram-negative bacilli may affect those who have recently used antibiotics, and anaerobes may affect wounds following the gangrene and ulcerations course. Samples obtained through biopsy from the wound site, debridement, and aspiration should be studied microbiologically. Tuberculosis infection should be considered in diabetic foot ulcer that is non-healing despite empirical antibiotic treatments.

The incidence rate of extrapulmonary tuberculosis infection is between 3.2% and 17.5% (12), while this rate for skin tuberculosis is reported as 1% among all other tuberculosis types in developed countries. The incidence of skin tuberculosis is parallel to that of pulmonary tuberculosis (13). Skin involvement may be accompanied by papules, plaques, nodules, abscesses, and ulcers (14).

EI is observed mostly in women and in the lower extremities (7). Our case was also a female patient with anterolateral lesions in the right lower extremity (Figure 1, 2).

The definitive diagnosis of tuberculosis is possible with cultivation of tubercle bacilli from clinical samples. The smear obtained from the collected materials allows for diagnosis of 50-90% of cases of pulmonary tuberculosis, and 25% of cases of extrapulmonary tuberculosis (15). A study by Marcoval and Alcaide (16) reported that PCR and other culture methods showed negative results in many cases. In the literature, most of the cases have not been reported to be with internal organ involvement. No tuberculosis bacillus was detected in the bronchoscopy samples or the skin biopsy obtained from our case either. Lesions regressed via tuberculosis therapy in a study of 20 patients, conducted by Scheinfeld et al. (17). They recommended anti-tuberculosis therapy and clinical follow-up of response to therapy in EI cases, even if bacillus is not observed. No bacillus was observed in this case either but the lesions fully regressed with a 6-month treatment regimen with 2 months of isoniazid, rifampicin, ethambutol, and pyrazinamide therapy and 4 months of isoniazid and rifampicin therapy.

Since tuberculosis infections are still an important public health issue in Turkey, especially in cases with chronic diseases such as diabetes; pulmonary and, particularly, more rarely observed extrapulmonary forms of the disease should be taken into consideration. In cases of resistant diabetic foot ulcer that do not respond to traditional treatment, tuberculosis infection should definitely be considered. It is recommended to apply anti-tuberculosis therapy and to follow-up clinical response to therapy in case of EI, even if bacillus is not observed.

Authorship Contributions

Informed Consent: Zühal Özer Şimşek, Concept: Zühal Özer Şimşek, Yasin Şimşek, Design: Zühal Özer Şimşek, Data Collection or Processing: Neslihan Cerrah Demir, Analysis or Interpretation: Yasin Şimşek, Hakan Büyükoğlan, Literature Search: Zühal Özer Şimşek, Writing: Zühal Özer Şimşek, Peer-review: External and Internal peer-reviewed, Conflict of Interest: No conflict of interest was declared by the authors. Financial Disclosure: The authors declared that this study has received no financial support.

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