



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

Öz

Eritema induratum Bazin Mikobakteriyum tüberkülozise karşı oluşan bir hipersensivite reaksiyonudur. Genellikle, iyileşmeyen yaralardan alınan deri biyopsilerinde etken gösterilememesi, kültürde üreme olmaması ve yaraların anti-tüberküloz tedaviyle gerilemesiyle tanı alır. Bu olguyu sunmada, standart tedavilerle iyileşmeyen diyabetik ayak yaralarında tüberkülozun da düşünülmesi gerekliliğini amaçladık.

Anahtar kelimeler: Diyabetik ayak yarası, tüberküloz, eritema 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.

Typical EI is characterized by repeated subcutaneous sensitive erythematous plaques especially in the lower extremities, typically in early adolescence and perimenopausal period, and by painful nodules that are ulcerated in the mid-regions (5,6,7). Generally, EI is diagnosed by a negative skin biopsy, negative culture of Mycobacterium tuberculosis and by regression of the lesions after anti-tuberculosis therapy. It becomes chronic if left untreated and new lesions form within 3-4 months (6,7,8). Over time, squamous cell cancer can develop from the scar tissue (9). Even if polymerase chain reaction (PCR) and other methods fail to demonstrate tuberculosis bacillus, 4-drug anti-tuberculosis treatment for 6 months is recommended. Erythema nodosum, often seen in the lower extremities, may be confused with cutaneous polyarteritis nodosa (PAN), subcutaneous sarcoidosis, and cutaneous T-cell lymphoma.

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/ μ L, 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 EI 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

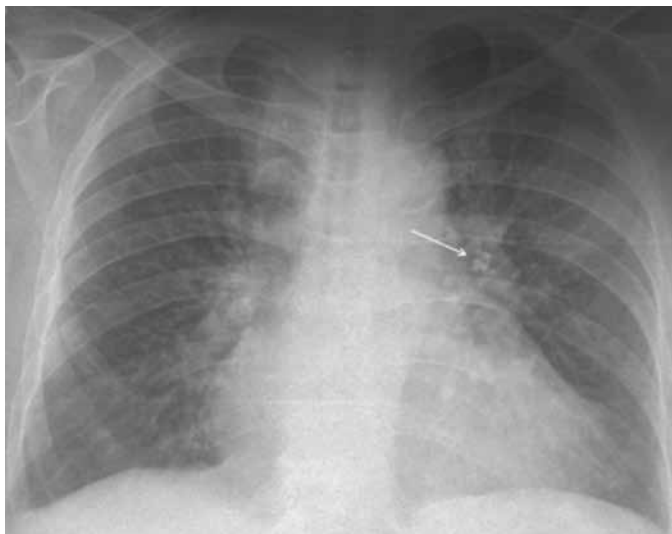


Figure 3. Left hilar calcificated appearance



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, abscess, 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 Scheinider 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.

References

- Kundakçı N, Taşpınar A. Lepre ve diğer mikobakteriyel deri infeksiyonları: Deri tüberkülozları. İçinde: Topçu AW, Söyletir G, Doğanay M, eds. İnfeksiyon hastalıkları. Nobel Tıp Kitabevleri; 1996:803-817.
- White WL. On Japanese baseball and erythema induratum of Bazin. Am J Dermatopathol 1997;19:318-322.
- Scheinfeld NS, James WD. Erythema Induratum (Nodular Vasculitis) clinical presentation. Medscape; 2012.
- Leow LJ, Pintens S, Pigott PC, Whitfield MJ. Erythema induratum - a hypersensitivity reaction to *Mycobacterium tuberculosis*. Aust Fam Physician 2006;35:521-522.
- Feiwel M, Munro DD. Diagnosis and treatment of erythema induratum (Bazin). Br Med J 1965;1:1109-1111.
- Rademaker M, Lowe DG, Munro DD. Erythema induratum (Bazin's disease). J Am Acad Dermatol 1989;21:740-745.
- Requena L, Sánchez Yus E. Panniculitis. Part II. Mostly lobular panniculitis. J Am Acad Dermatol 2001;45:325-361.
- Segura S, Pujol RM, Trindade F, Requena L. Vasculitis in erythema induratum of Bazin: a histopathologic study of 101 biopsy specimens from 86 patients. J Am Acad Dermatol 2008;59:839-851.
- Yates VM. Myco bacterial infections. In: Burns T, Breathnach S, Cox N, Griffiths C, eds. Rook's Textbook of Dermatology (8th ed) Oxford; Wiley-Blackwell; 2010;31:1-31.
- Boulton AJ. The diabetic foot: a global view. Diabetes Metab Res Rev 2000;16(Suppl 1):2-5.
- Smith DM, Weinberger M, Katz BP. A controlled trial to increase office visits and reduce hospitalizations of diabetic patients. J Gen Intern Med 1998;2:232-238.
- Kalaç N, Başay N, Mutluay Nİ, Bayız H, Özkul M. Ekstrapulmoner tutulum gösteren tüberküloz olguları. Tüberküloz ve Toraks 1999;47:213-215.
- Tüzün Y, Mat MC. Mikobakteri hastalıkları. İçinde: Tüzün Y, Kotoğyan A, Aydemir EH, eds. Dermatoloji. İstanbul; Cem Ofset Matbaacılık Sanayi; 1994:121-127.
- Dodiuk-Gad R, Dyachenko P, Ziv M, Shani-Adir A, Oren Y, Mendelovici S, Shafer J, Chazan B, Raz R, Keness Y, Rozenman D. Nontuberculous mycobacterial infections of the skin: a retrospective study of 25 cases. J Am Acad Dermatol 2007;57:413-420.
- Gupta A, Sharma SK, Pande JN. Diagnostic methods for tuberculosis. Indian J Chest Dis Allied Sci 1993;35:63-84.
- Marcoval J, Alcaide F. Evolution of cutaneous tuberculosis over the past 30 years in a tertiary hospital on the European Mediterranean coast. Clin Exp Dermatol 2013;38:131-136.
- Schneider JW, Jordaan HF, Geiger DH, Victor T, Van Helden PD, Rossouw DJ. Erythema induratum of Bazin. A clinicopathological study of 20 cases and detection of *Mycobacterium tuberculosis* DNA in skin lesions by polymerase chain reaction. Am J Dermatopathol 1995;17:350-356.