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Authors
Kandemir, S
Dezoteux, F
Loiez, C
et al.

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Diffuse skin findings secondary to lymph node tularemia in a patient with chronic rheumatoid arthritis on methotrexate

S Kandemir[1], F Dezoteux[2,3], C Loiez[4], T Hubiche[5], S Laurent[6], S Darras[1]

Affiliations: [1]Department of Dermatology, Hôpital Duchenne, Boulogne-sur-Mer, France, [2]Department of Dermatology, Lille University Hospital Center, Lille, France, [3]Institute for Translational Research in Inflammation, Lille University Hospital Center, Lille, France, [4]Department of Bacteriology, Lille University Hospital Center, Lille, France, [5]Department of Dermatology, Nice University Hospital Center, Nice, France, [6]Department of Pneumology, Hôpital Duchenne, Boulogne-sur-Mer, France

Corresponding Author: Stéphane Kandemir, Department of Dermatology, Hôpital Duchenne, 609 Allée Jacques Monod, Boulogne-sur-Mer, France Tel: 33-3-21-99-31-65, Email: stephane.kandemir@gmail.com

Abstract

Tularemia has many atypical presentations which can represent a diagnostic challenge. The history is essential in the investigation of this disease. Bite-induced primary skin lesions should be distinguished from the infrequent immune-mediated secondary skin lesions. Herein, we present an atypical pseudovesicular rash secondary to *Francisella tularensis*.

Keywords: adenopathy, case report, immunosuppressed, skin, tularemia

Introduction

Tularemia is a zoonotic disease caused by *Francisella tularensis*, a Gram-negative intracellular bacterium [1]. It is an agent of bioterrorism and in most countries in Europe, a reportable disease [1]. *F. tularensis* has many animal reservoirs, including small rodents and lagomorphs, arthropods, and mosquitoes [1]. Three major modes of transmission to humans exist: directly from the animal reservoir, arthropod bites and transmission through contaminated water, soil environments or inhalation[1–4]. Tularemia has a short incubation period of 3-5 days and has six major clinical forms recognized, depending on the portal of entry of bacteria [1–4]. There are the ulceroglandular and the glandular forms (more than 95% of the outbreaks), the oropharyngeal form, the oculoglandular form, the respiratory form and the thyphoidal form (each one represents less than 1%), [5]. Tularemia complications might include skin rashes including erythema nodosum, erythema multiforme, maculopapular rashes or rarely vesicular eruptions [1,4,6,7]. Herein we present a case of the respiratory form of tularemia complicated by targetoid-like and atypical pseudovesicular skin lesions.

Case Synopsis

A 63-year-old man, a ranger, was hospitalized for altered general condition with hyperthermia. He had a medical history of rheumatoid arthritis treated with methotrexate (MTX) 10mg once a week for 10 years. Six weeks earlier, he picked up a freshly dead hare with his bare hands that had been run over by a car during one of his walks. Prodromal symptoms including fever and cough started a few days after his walk and the general practitioner tried a five-day amoxicillin treatment that was ineffective. Approximately 10 days after the beginning of the prodromal symptoms the patient noticed the appearance of erythematous macules, non-pruritic pseudovesicles, and papules located on the back and proximal part of the arms, as well as slightly infiltrated targetoid-like lesions of the hands (**Figure 1**). All the lesions occurred within 24 hours. HIV, leptospirosis, and syphilis serologies were negative. Autoimmune and angiotensin converting enzyme tests were normal. A CT scan was performed (**Figure 2**), showing a non-specific bronchial thickening and

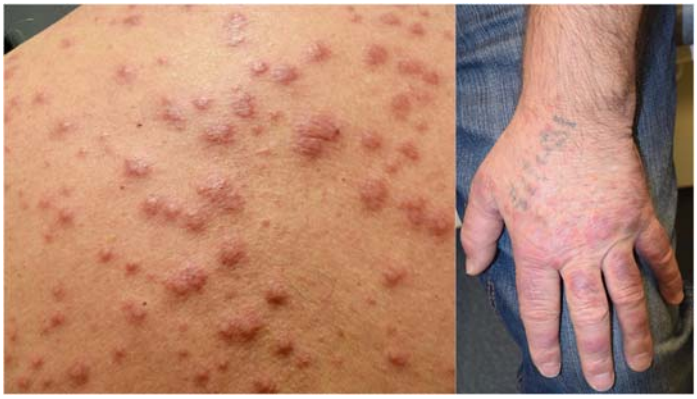

Figure 1. *Erythematous papule and pseudovesicles on the back and papule on the right hand before treatment.*

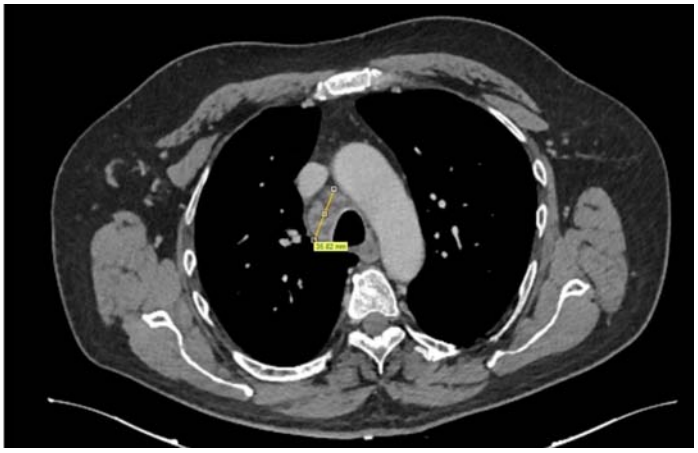

Figure 2. *Necrotic mediastinal adenopathy of 3.5cm.*

necrotic mediastinal lymph nodes, mainly suggestive of the diagnosis of tuberculosis or sarcoidosis, but there was no pulmonary infiltrate. Skin biopsy (**Figure 3**) revealed non-specific edema with interface dermatitis, polymorphic perivascular infiltrate, and periodic acid-Schiff was negative. Fine needle aspiration biopsy was performed by bronchial echo endoscopy (EBUS) that collected a purulent liquid. Acid-fast bacilli staining and cultures were negative but the PCR for *F. tularensis* was positive on the liquid collected by EBUS. Then, we performed a positive tularemia serology which confirmed the diagnosis with a positive titer of immunoglobulin G level at 1/640 and immunoglobulin M level at 1/320 (normal titer below 1/80). Retrospectively, *F. tularensis* PCR was performed on the skin biopsy but it was negative. Treatment with levofloxacin 500mg twice a day was started for 15 days. We saw the patient two days after the end of his treatment and noted the healing of his lesions with the appearance of post-inflammatory hyperpigmented scars (**Figure 4**). The general signs have also regressed.

Case Discussion

Tularemia is an endemic, potentially fatal zoonosis caused by the bacterium *F. tularensis* [1]. Our case is original because it is an uncommon respiratory form of tularemia associated with an immune-mediated secondary skin lesion [5]. The transmission in these cases is by inhalation of bacterial aerosols through the carcasses of lagomorphs [5]. Syrjala et al. found more hilar adenopathy than pulmonary infiltrate in his series of 38 respiratory tularemia cases [8]. The mediastinal involvement can mimic lung cancer but EBUS helped us to correct the diagnosis as in the series of Fachinger et al. who diagnosed four cases of tularemia by EBUS mistaken for lung cancer [9]. Secondary skin involvement is infrequent (20%) and mainly represented by erythema nodosum, erythema multiforme, or nonspecific maculopapular

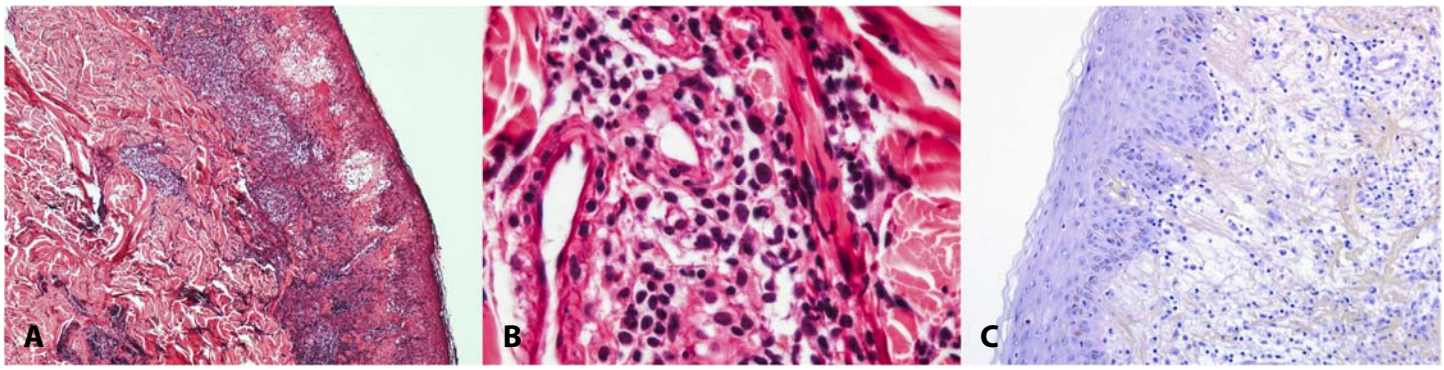

Figure 3. *H&E histopathology of biopsy **A)** displaying edematous papillary dermis, 40×; **B)** displaying perivascular infiltrate, 400×. **C)** Negative periodic acid-Schiff stain of biopsy displaying edematous papillary dermis, 200×.*

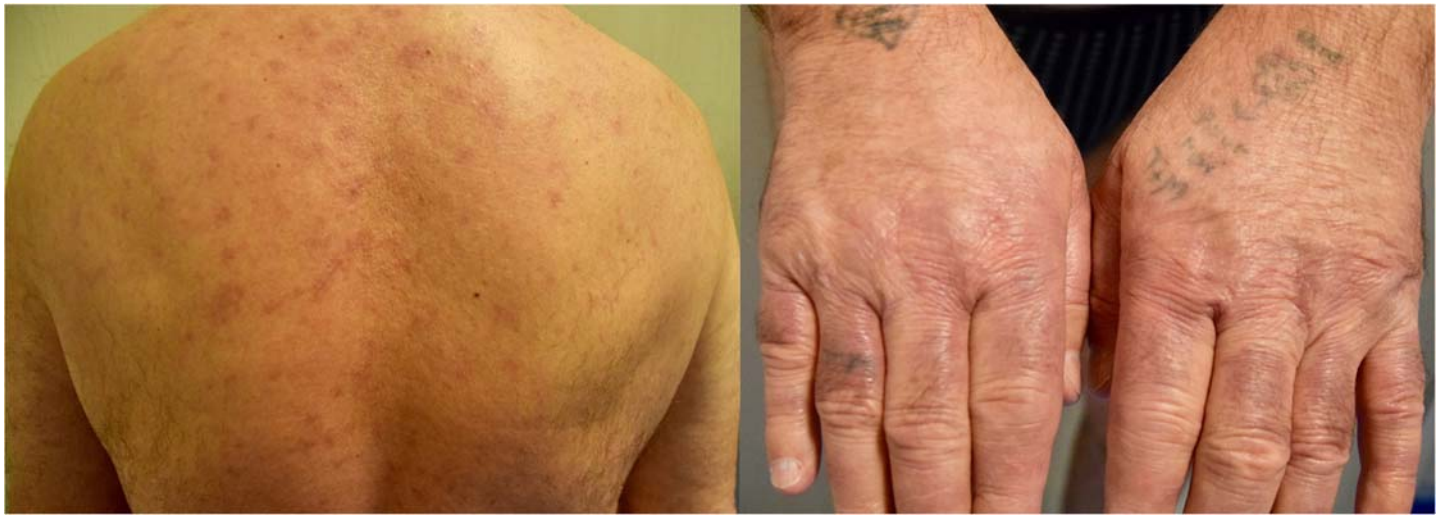

Figure 4. *Back and hand after treatment with levofloxacin.*

rashes [1,3,4,10]. Vesicular lesions are uncommon cutaneous manifestations of tularemia with few reports since the first documented cases of vesicular tularemia [7]. Eliasson et al. noticed 7 (3%) vesicular eruptions in their series of 234 tularemia cases [4]. Byington et al. warned about misdiagnosis of culture-positive tularemia vesicular skin lesions with herpes simplex virus or varicella-zoster virus [6]. Macquart et al. described a similar case to ours in a microbiologist who inhaled *F. tularensis* in his laboratory with lower lobe pneumonia, adenopathy, vesicular skin lesion, and erythema nodosum [7]. The infiltrated papular lesions of the hands are qualified by some authors as tularemids as are lesions secondary to syphilis [11]. Our case is original by the diagnostic method (EBUS) and the severity related to the immunodepression induced by the MTX justifying stopping the treatment. Skin biopsy is non-specific with interstitial and perivascular inflammation or infiltrate, leucocytoclasis, and marked edema in the papillary dermis [2,7,10]. Serology remains the reference diagnostic test [1,5]. Frequently used antibiotic treatment for tularemia in Europe are: fluoroquinolones with ciprofloxacin 500mg twice daily, levofloxacin 500mg once a day over two weeks, tetracyclines especially doxycycline 100mg twice daily over three weeks, or aminoglycosides with gentamicin 5mg/kg intravenously in one or two doses for duration of ten days [1,5]. We opted for levofloxacin which allowed the patient to heal without recurrence.

Conclusion

Any erythematous rash in the context of a rural lifestyle or walks in the woods should lead the clinician to think about the diagnosis of tularemia. Because of the risk of biological terrorism and items in the differential diagnoses such as lung cancer or tuberculosis, it is essential to recognize it and avoid misdiagnosis and prescription of an inadequate treatment.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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