

# Eschar in a Belgian traveler returning from Central Europe

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## Abstract

**Background:** Tularemia is a zoonotic infection caused by *Francisella tularensis*, an aerobic, facultative intracellular coccobacillus, encountered especially in the Northern hemisphere. *F. tularensis* is a pathogen of humans and hundreds of animal species. **Patients and methods:** A Belgian traveler returning from an adventurous vacation in Central Europe presents fever, flu-like symptoms, a skin ulcer with a necrotic center resembling an eschar on the left thigh and painful left inguinal lymphadenopathy. An enzyme linked immunosorbent assay developed by the National Reference Laboratory for Tularemia, Sciensano, Belgium, detected elevated Ig G antibodies against *F. tularensis*, while the rest of the serologies were negative. **Results:** A highly likely case of ulceroglandular tularemia is described and the differential diagnosis is discussed. **Conclusion:** The incidence of tularemia has been increasing throughout Europe in recent years. Physicians should be aware of this disease, its diversity of reservoirs, transmission routes and clinical presentations.

## INTRODUCTION

Tularemia is a zoonotic infection caused by *Francisella tularensis*, a non-motile, aerobic, facultative intracellular pleomorphic Gram-negative coccobacillus, which can infect numerous vertebrate and non-vertebrate species [1–4]. In Europe there are natural foci of tularemia in forests and grasslands, where lagomorphs (e.g. hares, rabbits, ...) and rodents (e.g. mice, rats, squirrels, ...) are the principal vertebrate hosts. The tick *Dermacentor reticulatus* is the principal vector and reservoir [2]. Humans can be infected either through direct contact with infected animals (such as hares or rabbits) or carcasses, by arthropod bites (such as ticks, fleas, or mosquitos), by ingestion of contaminated food or water or by inhalation of contaminated aerosols [2–4]. The bacteria enter through injured skin or conjunctival, oral, or respiratory mucosae and, after a short incubation period of 3–5 days on average, (range 1–21 days), patients develop flu-like symptoms [2]. Depending on the portal of entry, patients will develop one of five clinical syndromes: ulceroglandular, glandular, oculoglandular, oropharyngeal, pneumonic or typhoidal tularemia [1–4]. Ulceroglandular tularemia, characterized by a combination of skin ulceration and regional lymphadenopathy, is the most common form (>80%) [5].

## CASE REPORT

A 54-year-old Belgian male was referred to the Emergency Department with fever, night sweats, fatigue, neck pain, an eschar on

the left thigh and painful left inguinal lymph nodes, 3 days after returning from a 2-week adventurous trip in the forests of Central Europe (Austria, Germany, northern Italy and Slovenia). The fever had begun one week earlier, while on vacation. On return he was prescribed amoxicillin-clavulanate by his general practitioner, without improvement. The following day he noticed an ulcer on his left thigh, which he attributed to a mosquito bite. On further questioning he reported hiking and camping in the woods and contact with water while kayaking, but no tick bite nor contact with wild animals. He owned a cat, and his medical history was unremarkable. His clinical examination was normal, except for tachycardia (102 beats per minute), an erythematous lesion with a necrotic center resembling a 'tache noire' on the left thigh (Fig. 1—eschar) and painful left inguinal lymphadenopathy. Laboratory examinations revealed a normal leukocyte count ( $7.6 \times 10^9/L$ ) and a C-reactive protein level of 26 mg/L (reference < 5 mg/L). Amoxicillin-clavulanate was discontinued, doxycycline was initiated to treat a potential tick-borne disease and additional blood tests were carried out. Twelve days later the patient returned to the outpatient clinic in an improved condition: the fever had subsided, the eschar was healing, but the lymphadenopathy persisted. Blood cultures were negative. Serologies for *Bartonella henselae*, *Rickettsia conorii*, *Rickettsia mooseri/typhi* and *Borrelia* were negative. Additional laboratory analysis (enzyme linked immunosorbent assay developed by the National Reference Laboratory for Tularemia, Sciensano, Belgium) detected elevated Ig G antibodies against *F. tularensis*. No polymerase chain

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**Figure 1.** Eschar on the patient's left thigh.

reaction was performed on the eschar. The patient fully recovered after a 14-day course of doxycycline and no repeat serology was performed.

## DISCUSSION

This patient with highly likely ulceroglandular tularemia presented with an eschar (or 'tache noire') after returning from an adventurous vacation in Central Europe. Such lesions are characteristic of Mediterranean spotted fever ('fièvre boutonneuse'), a tick-borne disease mainly distributed around the Mediterranean basin, in Sub-Saharan Africa and Asia. Mediterranean spotted fever is caused by an intracellular bacterium, *R. conorii*, and the eschar represents the local vasculitis with secondary skin necrosis at the entry point of the bacteria. In this case, the patient did not recall a tick bite, *F. tularensis* antibodies were elevated and the other serologies were negative. While rare, co-infections *F. tularensis*/*Rickettsia* spp. are described [6]. Although improbable, this is not entirely ruled out in our case, as initial *Rickettsia* serology can be negative in the spotted fever group and no repeat serology was performed. Lesions resembling a 'tache noire' have also been reported in other infections, such as Q fever [7]. Other etiologies to be considered in case of ulcers or eschars accompanied by local adenopathy are ecthyma, herpes simplex infections, cat scratch disease, tick-borne borreliosis, anthrax, mycobacterial infections, syphilis, venereal granuloma, leishmaniasis or ehrlichiosis [5]. According to the World Health Organization definitions of tularemia, potential cases are defined as patients with suggestive clinical symptoms and either positive serology or positive DNA detection in one clinical sample, infections are confirmed when an *F. tularensis* strain can be isolated and identified in culture, or by a 4-fold increase in antibody titers (IgM or IgG) in paired serum specimens [8]. However, because DNA detection techniques are not readily available in all regions, and culture-based techniques for *F. tularensis* require a Biosafety Level 3 laboratory [2], the diagnosis is primarily based on suggestive clinical and epidemiological data and positive serology [3]. In our patient, who responded rapidly to doxycycline, no control blood work was required and therefore no paired serology was performed. The tularemia diagnosis corresponded with the clinical presentation, the visited regions and the outdoor activities in which he had engaged, and previous infection (and thus seropositivity) was unlikely. The European continent has seen an increase in human tularemia cases in recent years [9]. In 2021 there were 876 confirmed cases of human tularemia, equaling 0.20 per 100 000 population, and thus an increase of 42.9% compared with the

average annual notification rate from 2017 to 2019 (data from the United Kingdom excluded) [9]. All four countries visited by the patient reported increased number of cases in 2021, with Slovenia having the second-highest notification rate in the European Union, after Finland [9]. This emphasizes the need for sensitization to tularemia risks and prevention of certain professional groups such as hunters, foresters, furriers, military personnel, and of tourists particularly interested in nature, agritourism or water recreationists [10]. Physicians must be aware of the risk factors, the particular risk groups and the diversity of clinical presentations of tularemia. The antibiotics of choice are fluoroquinolones, aminoglycosides and tetracyclines [3]. Considering that untreated tularemia can lead to complications including endocarditis, meningitis and even death, early empiric treatment with a broad-spectrum antibiotic that also covers other tick-borne bacteria such as doxycycline needs to be considered.

## CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

## FUNDING

None.

## ETHICAL APPROVAL

Case reports are waived by the Ethics Committee of our institution.

## CONSENT

The patient provided written consent for publication of the case report and accompanying images.

## GUARANTOR

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