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Evaluation of tularaemia courses: a multicentre study from Turkey

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Abstract

In this multicentre study, which is the largest case series ever reported, we aimed to describe the features of tularaemia to provide detailed information. We retrospectively included 1034 patients from 41 medical centres. Before the definite diagnosis of tularaemia, tonsillitis (n = 653, 63%) and/or pharyngitis (n = 146, 14%) were the most frequent preliminary diagnoses. The most frequent clinical presentations

were oropharyngeal (n = 832, 85.3%), glandular (n = 136, 13.1%) and oculoglandular (n = 105, 10.1%) forms. In 987 patients (95.5%), the lymph nodes were reported to be enlarged, most frequently at the cervical chain jugular (n = 599, 58%), submandibular (n = 401, 39%), and periauricular (n = 55, 5%). Ultrasound imaging showed hyperechoic and hypoechoic patterns (59% and 25%, respectively). Granulomatous inflammation was the most frequent histological finding (56%). The patients were previously given antibiotics for 1176 episodes, mostly with β-lactam/β-lactamase inhibitors (n = 793, 76%). Antituberculosis medications were provided in seven (2%) cases. The patients were given rational antibiotics for tularaemia after the start of symptoms, with a mean of 26.8 $\pm$ 37.5 days. Treatment failure was considered to have occurred in 495 patients (48%). The most frequent reasons for failure were the production of suppuration in the lymph nodes after the start of treatment (n = 426, 86.1%), the formation of new lymphadenomegalies under treatment (n = 146, 29.5%), and persisting complaints despite 2 weeks of treatment (n = 77, 15.6%). Fine-needle aspiration was performed in 521 patients (50%) as the most frequent drainage method. In conclusion, tularaemia is a long-lasting but curable disease in this part of the world. However, the treatment strategy still needs optimization.

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Introduction

Tularaemia is a zoonotic infection caused by *Francisella tularensis*, and the disease has been seen in many parts of the northern hemisphere [1,2]. *F. tularensis* is a very potent human pathogen that can produce infection with as few as ten organisms. The microorganism is highly infectious, and may enter the human body through the skin after contact with an infected animal; transmission through the mucosal membranes of the mouth, throat, eye or bronchus may also occur. Furthermore, ticks can also transmit the pathogen [3]. The disease has various clinical presentations, including ulceroglandular, glandular, oculoglandular, oropharyngeal, pneumonic and typhoidal forms [3]. The ulceroglandular form of the disease has been reported to be the most common form in the USA and European countries such as Bulgaria, Hungary, Austria, and Germany [4,5]. The bacterium is known to persist in water, hay or mud for weeks, and waterborne epidemics have been reported in eastern Europe and Turkey [6–9].

F. tularensis ssp. *tularensis* (type A) and *F. tularensis* ssp. *holarctica* (type B) are the two major subspecies causing human disease. Type A is considered to be a potential agent of biological warfare, as it is highly infectious and can cause severe disease with high fatality rates [10]. On the other hand, type B causes mild disease with low fatality rates in Europe and Asia, and is occasionally related to waterborne tularaemia outbreaks. Both climate change and global warming have been suggested to have contributed to the spread of the disease [11]. Recent outbreaks and sporadic case notifications of tularaemia have been observed in Europe [12]. Sporadic cases of tularaemia or local outbreaks have been reported since 1936 in Turkey, and the disease has been increasingly seen in Turkey since 1988 [13]. The clinical manifestations of tularaemia have been reported to range from asymptomatic illness to septic shock [3]. As tularaemia has been known to be potentially fatal if left untreated [14], proper management of the disease is of paramount importance for the patient.

There are relatively small case series for tularaemia in the medical literature detailing the features and the management issues for the disease. Thus, in this multicentre study, which is the largest case series ever reported, we aimed to delineate the potential impacts of this multifaceted disease, and to provide detailed information concerning the clinical, diagnostic and therapeutic implications of tularaemia in a region of the northern hemisphere, Turkey.

Materials and Methods

Study design and patient population

This multicentre study pooled patients with any form of tularaemia from 41 medical centres in Turkey. The cities of the participant centres are shown in Fig. 1. The study had a retrospective design, and included patients treated between 2000 and 2013. No control groups were included for this study. Fatih Sultan Mehmet Training and Research Hospital's Review Board in Istanbul approved the study.