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Original Contribution

Predicting tularemia with clinical, laboratory and demographical findings in the ED☆

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ABSTRACT

Introduction: We aimed to determine clinical, laboratory and demographical characteristics of tularemia on admission to Emergency Department (ED).
Material and Methods: Medical data of 317 patients admitted to ED and subsequently hospitalized with suspected tularemia between January 1, 2011, and May 31, 2015, were collected. Patients were divided into 2 groups according to microagglutination test results, as tularemia (+) and tularemia (−).
Results: Of the 317 patients involved, 49 were found to be tularemia (+) and 268 were tularemia (−). Mean age of the tularemia (+) patients was found to be higher than that of tularemia (−) patients. When compared to tularemia (−) patients, a significant portion of patients in tularemia (+) patients were elderly, living in rural areas and had contact with rodents. When clinical and laboratory findings of the 2 groups were compared, any statistical significance could not be determined.
Conclusion: Tularemia is a disease of elderly people living in rural areas. Contact with rodents also increases risk of tularemia in suspected patients.

1. Introduction

Tularemia is a zoonotic disease caused by a a highly infectious, facultative intracellular, Gram-negative coccobacillus named *Francisella tularensis*. The disease is common in Turkey and throughout the World, particularly in North America, Europe, and Asia. It is also known as “rabbit fever”, “hunters’ disease”, “deerfly fever”, “tick fever”, “O’Hara’s Disease” and “Francis’ Disease” [1–3].

Transmission of the disease to humans occur through tick bites, contact with contaminated animals, consumption of infected animals’ meat, drinking contaminated water, and inhalation [4,5]. Even though a definitive reservoir has not been determined, arthropods, birds, rodents, lagomorphs, carnivores and ruminants, are known to carry *Francisella*[6].

Depending on the route of exposure and type of bacteria, clinical presentation of the disease vary from mild skin lesions and lymphadenopathy to pneumonia and/or septicemia which threatens life [7].

The main forms of the disease are ulceroglandular, glandular, oculoglandular, oropharyngeal, pneumonic, and typhoidal (septicemic). The majority of the cases in Europe and Turkey are known to be in the form of oropharyngeal tularemia [2]. Oropharyngeal tularemia is characterized by swollen ear, nose and throat lymph nodes develops after the ingestion of the bacterium, and oculoglandular tularaemia when eyelids and other periorbital structures are infected, usually through aerosols or contact with fingers carrying the bacterium [8].

Due to infection capacity of *F tularensis* in low doses and ease of dissemination by aerosols, it is also used as a biological weapon, hence this bacterium was categorized as a highly dangerous biological agent by the Centers for Disease Control in Atlanta, Georgia [3].

In this article, we aimed to determine clinical and laboratory features of tularemia on admission in the Emergency Department (ED) and clarify predictors of the disease in order to prevent misdiagnoses.

2. Material and methods

Medical data of 317 patients admitted to ED of Hitit University Çorum Education and Research Hospital with suspected tularemia between January 1, 2011, and May 31, 2015, were collected, retrospectively. Presumeptive diagnosis of tularemia on admission to ED was based on suspicion of the clinicians in patients with regional

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lymphadenopathy, painful maculopapular lesions, rodent and/or tick exposure, unexplained fever and symptoms of upper respiratory system disorders. Suspected patients were hospitalized after Infectious Diseases consultation. From the medical records of the patients, initial clinical and laboratory characteristics in ED were collected. Then, tularemia test results for tularemia microagglutination (MA) titration of the patients were collected. Patients were divided into two subgroups according to test results as tularemia (+) and tularemia (−). Two groups were compared according to clinical and laboratory findings. Patients were investigated for age, complaints on admission, location, occupation, properties of water used for drink, contact with animals, tick bite, farming, contact with rodents, family or neighbourhood history for similar diseases and outcome (hospitalization, transfer to an advanced center or death). For definite diagnosis of tularemia, agglutination titrates were studied from blood serum samples of the patients. In patients with agglutination titrates above 1:160, those with positive polymerase chain reaction or cultural reproduction were confirmed as tularemia. Statistical analyses were performed using SPSS 22.0. Descriptive data were given as arithmetic mean ± standart deviation, minimum-maxiumum and percentages. For statistical evaluation χ^2, Mann-Whitney *U* tests, and stepwise logistic regression analysis were used. p < 0,05 was considered statistically significant.

3. Results

Of the 317 patients involved, 49 (15.5%) were found to be tularemia (+) and 268 (84.5) were tularemia (−). When distribution of the tularemia (+) patients in according to years was investigated, it was found that 9 patients (18,4%) in 2011, 14 patients (28.6%) in 2012, 10 patients (20.4%) in 2013, 13 patients (26.5%) in 2014, and 3 patients (6.1%) in the first half of 2015 were tularemia (+). A statistical significance could not be found in incidence according to years ($P > .05$).

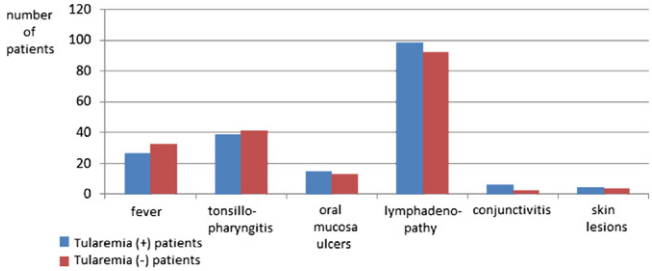
While 36.7% of the tularemia (+) patients was male, 45.5% of the tularemia (−) patients was male ($P > .05$). Mean age was 42.7 ± 15.1 (min:6-max:81) in tularemia (+) and 36.0 ± 21.1 (min,0; max,94) in tularemia (−) patients. This finding was found to be statistically significant. In tularemia (+) group, 14.3% of the patients were between 0 and 5 years of age, 8.2% were students and 8.2% were in agriculture agriculture work. In tularemia (−) group, 10.8% were between 0–5 years of age, 7.5% were students, and 5.6% were in agriculture work. When occupational status of the groups were compared, a statistical significant difference could not be found ($P > .05$). When living environment (rural area or city center) of the groups were compared, it was determined that 65.3% of the tularemia (+) patients were living in rural areas while 31.3% of the tularemia (−) patients were living in rural areas. This finding was also statistically significant ($P = .000$). Majority of the tularemia (+) patients was living in rural areas. Only in 4 villages, 2 or more cases were determined.

No significant differences were found between those patients with tularaemia and those without, with regard to such symptoms as sore throat, fever, myalgia, nausea anorexia lymphadenopathy, oral or skin ulceration, nor between tularaemia and contact with livestock, ground game, outdoor activities or tick bites ($P > .05$). Table 1 summarizes the comparison of clinical findings of groups on admission. We also could not determine any statistical significance between patients admitted to the hospital and those discharged to home according to their demographical, clinical and laboratory characteristics.

In logistic regression analysis, living in rural areas and contact with rodents were found to have statistical significance ($P = .000$, OR: 0.19, 95% CI [0.08-0.4]; $P = 0.02$, OR: 9.4, 95% CI [1.3-66.2], respectively). Parameters involved in the logistic regression analysis are summarized in Table 2.

When types of tularemia were investigated it was determined that majority of the cases was glandular form (n = 25, 51%) followed up by oropharyngeal form (n = 19, 38.8%), oculoglandular form (n = 1, 2%) and ulceroglandular form (n = 1,2%), respectively. Of 3 patients

Table 1
Comparison of clinical findings of groups on admission



(6.1%), clinical definite diagnosis could not be made. While 47 of the tularemia (+) patients (95.9%) were followed up as outpatients, 2 of them (4.1%) were hospitalized. On the other hand, 228 (85.1%) of tularemia (−) patients were followed up as outpatients and 40 (14.9%) were hospitalized.

Any statistical significance in regards to laboratory findings could not be determined between two groups.

4. Discussion

Tularemia is a zoonosis caused by the bacterium *F tularensis*; the main forms of disease that occur in humans are ulceroglandular/glandular, oculoglandular, oropharyngeal, and respiratory. In Turkey, tularemia outbreaks were described as early as 1936 to 1938, but tularemia was not reportable until 2004. Recently, multiple tularemia outbreaks in Turkey have been described, including in regions where the disease has not been previously reported; it is now considered a reemerging zoonotic disease in Turkey [9,10]. The only *F. tularensis* subspecies found in most of Eurasia, including Turkey, is *holarctica*[11,12]. Our study revealed that incidence of the disease does not increase significantly by years. This finding also demonstrates that we could not achieve a significant decrease in incidence of the disease, as well. So, more rigorious measures must be taken in warfare against tularemia.

In the literature, oropharyngeal form of tularemia is reported to be more common in Turkey than in other countries. In contrast, the ulceroglandular form is the most common type of tularemia in other countries; it is caused by blood-sucking insects or arthropods. The oropharyngeal form of tularemia is common in regions dominating aquatic cycle and is caused by the consumption of contaminated water or food. Urine, excrement or other excretions of animals involved in the aquatic cycle such as beaver, muskrat, and voles can contain the causative agent and infect surface waters after rainfall in the winter months. The main reason for the oropharyngeal form is the consumption of contaminated water by people [1,13]. Our finding that tularemia is more frequently seen in rural areas is compatible with the fact that contamination of water and contact with contaminated meat and animals are more frequent in rural areas. This finding shows that education of people in rural areas play an essential role in warfare against tularemia.

The clinical manifestations of tularemia depend on the route through which the bacterium entered the body and are usually ulceroglandular or typhoidal, although oculoglandular, oropharyngeal, and pneumonic forms have also been reported [14]. The ulceroglandular form, which represents 75 to 85% of all tularemia cases, corresponds to a regional lymphadenopathy with a painful maculopapular lesion that evolves to an eschar at sites of skin infection; it can also occasionally develop into systemic disease with a 5 to 15% case fatality rate [15]. In ED diagnosis of tularemia is based on suspicion of clinicians as it represents a wide range of symptoms mimicking other common diseases. It is known that up to 68% of the patients may initially be diagnosed with more common but clinically similar infections other than tularemia, particularly gram-positive lymphadenitis or cellulitis, cat-scratch disease, and Epstein-Barr virus infection [16].