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A small outbreak of tularemia in a rural area

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Aim: To assess clinically and epidemiologically an outbreak of tularemia detected in a small village in Tokat Province in Turkey.

Materials and methods: Recorded clinical and laboratory data of 15 serologically confirmed patients, who either presented to hospital or were diagnosed during family medicine visits to the village during the outbreak, were assessed. Forms including a questionnaire about the symptomatology and previously given treatments were filled out by the patients. In addition, the entire village was investigated to establish the origin of the outbreak.

Results: Ages of the 15 individuals (9 females) ranged between 10 and 75, and the mean was 34.2 ± 12.4. Thirteen patients matched the oropharyngeal type and 2 the oculoglandular type. The field investigation of the village revealed that open-air drinking water sources were not sufficiently chlorinated, and the villagers used to consume natural spring water. The outbreak was controlled via chlorination, with advice to the people to use clean water sources and limit natural spring water consumption.

Conclusion: Tularemia has become an emerging infection particularly due to the increase in water- and food-based outbreaks in recent years. The crucial step in its diagnosis is the clinical suspicion of tularemia since it is still an underestimated disease in Turkey. Therefore, clinicians should be informed about where the entity is common. It is suggested that safe drinking water sources should be provided by the authorities, and open-air natural spring water sources should be avoided for the control of outbreaks.

Key words: Tularemia, outbreak

1. Introduction

Tularemia is a zoonosis that is caused by *Francisella tularensis*. *F. tularensis* is a gram-negative, nonmotile, and strictly aerobic coccobacillus (1). The most common subspecies found in Turkey is *F. tularensis* biovar holarctica (type B). This biovar, which is usually responsible for oropharyngeal tularemia, has low virulence and clinical features of the disease are milder than those of other biovars (2,3). Infection can occur via ingestion or inhalation of *F. tularensis* or contact with infected animals such as rabbits, mice, or rats or it can be tick-borne (3–5). Epidemics can occur in both humans and animals. In recent years, increases in the number of outbreaks and cases have been observed in various regions of Turkey. According to Health Ministry data, the number of cases in 2005 was 374 and it exceeded 1000 cases by the end of the first half of 2010 (6). In the present study, we examined the clinical and epidemiological features of a tularemia outbreak that appeared to be waterborne and that affected 15 patients in a district of Tokat.

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2. Materials and methods

Two male patients aged 13 and 16 from the same family presented to the infectious diseases outpatient clinic of a state hospital in May 2010 with fever, sore throat, loss of appetite, and cervical swelling. Tularemia was suspected clinically and the patients were given tularemia treatment after serum samples were taken. In the following days, 7 more patients from the same district presented to our hospital with similar complaints. The district where the outbreak occurred was visited and 6 more patients were identified who had been diagnosed with tularemia and treated and followed-up by medical centers in other cities. An infectious diseases specialist interviewed all patients and filled out a questionnaire with regard to the onset of the disease, signs and symptoms, any kind of treatment before the diagnosis, duration of the diagnosis process, and any laboratory data that were available. In the meantime, water samples were taken to identify the source of the infection. Diagnoses of the patients who presented to our hospital and those followed-up by other centers were established at Refik Saydam National Public Health Agency by *F.*

tularensis microagglutination test (MAT) using serum samples sent by the Local Health Authority.

3. Results

Mean age of the 15 patients was 34.2 ± 12.4, within the age range of 10–75 years. There were 6 males and 9 females. All patients were residents of a district some 15 km away from the town center. Thirteen cases conformed to oropharyngeal tularemia and 2 to oculoglandular tularemia. Most of the patients were prescribed beta-lactam antibiotics, especially for tonsillo-pharyngitis before being diagnosed with tularemia. Various clinical and epidemiological features of the patients are presented in the Table.

F. tularensis MAT titers were 1/160 and over in 12 and 1/80 in 3 patients. Nine patients who were followed-up in our hospital were given streptomycin treatment. Of the remaining 6 patients, 3 received streptomycin and 3 were given streptomycin and doxycycline. Eight patients in whom the time between the onset of symptoms and diagnosis was less than 3 weeks made a full recovery, whereas cervical lymphadenopathy persisted despite antimicrobial treatment when the duration was longer than 3 weeks in 7 patients. These patients were referred to the ear, nose, and throat outpatient clinic for treatment and follow-up.

Investigation of the district revealed that 6 patients were from the same neighborhood and 3 were from the same family. We also noted that the water was not chlorinated regularly and the tap water was turbid after rain. Tests carried out in the Public Health Laboratory showed that the chlorine concentration of the tap water was insufficient and that the water was contaminated with copious amounts of *E. coli*. *F. tularensis* was not detected in samples analyzed by the Local Health Authority. At a location in the district, a natural spring and small water channels were noted. Residents had been using this water for domestic purposes although they did not drink it.

Chlorination of the water was carried out to control the outbreak. Doctors and other staff at the Family Health Center were given training to educate the residents and the residents were advised not to use spring water. No other tularemia case was observed until January 2011, when the author took up a post at a hospital in another area.

4. Discussion

Tularemia was first described by McCoy as a disease of squirrels in the Tulare region of California. In later years, the cause of tularemia, *F. tularensis*, has been shown to be pathogenic in humans as well. The first tularemia epidemic in Turkey occurred in 1936, in a military facility in Lüleburgaz and outbreaks have been recorded in different regions since then (2). In 2004 and 2005, large-scale outbreaks occurred especially in the Western Black Sea and Marmara regions (7,8). Tularemia has been included among notifiable diseases in 2005 and tularemia outbreaks have been reported in 35 cities since. In the first half of 2010, more than 1000 cases were reported in 32 cities (2,6).

Table. Various features of the patients with tularemia.

Clinical and epidemiological features	Frequency (%)
Sex: Male	6
Turbidity of tap water	15
Presence of similar complaint in the same family	3
Fever	15
Sore throat	13
Ophthalmic findings	2
Cervical swelling	15
Diarrhea	5
Loss of appetite	10
Weight loss	4
Inappropriate antibiotic treatment before diagnosis	11
Length of diagnosis <3 weeks	8
Uncomplicated recovery	8

In the present study, we reviewed a tularemia outbreak that affected 15 patients, 9 of whom were followed-up in our hospital. Most of the outbreaks in Turkey are thought to be due to contaminated water and food (7–11). Even though we failed to detect *F. tularensis* in water samples, we found that the drinking water was not adequately chlorinated and spring water had been used for various reasons. These suggest that the mode of contamination in this outbreak was water. The small number of bacteria identified in water sources makes identification of the microorganism difficult. Waters suspected to be the source of the disease were analyzed and DNA of the pathogen was identified by polymerase chain reaction in some outbreaks, while the cause of the outbreak could not be identified in others, as in the present case (4,12,13). Obtaining as much water as possible is recommended to identify the pathogen (12).

Waterborne tularemia outbreaks usually occur in autumn and winter, although this outbreak occurred in summer after a rainy spring (14). Contamination of the drinking water after heavy precipitation might have contributed to the occurrence of the outbreak.

Tularemia may present itself via various clinical manifestations, depending on the virulence of the bacteria, port of entry, extent of the systemic involvement, and immune status of the host. There are 6 forms of tularemia, namely ulceroglandular, glandular, oculoglandular, oropharyngeal, typhoidal (systemic), and pneumonic (3,14). While the most common form worldwide is the ulceroglandular form, oropharyngeal tularemia comprises the majority of cases in Turkey (7–9,15–17). In oropharyngeal tularemia, fever and sore throat develop after an incubation period of 3–5 days. Membranous tonsillitis and usually unilateral cervical lymphadenopathy may be observed during physical examination (14). Cervical lymphadenopathy has been reported as the main symptom in most cases during an outbreak, whereas fever, cervical lymphadenopathy, and membranous tonsillitis have been detected in all 13 cases of oropharyngeal tularemia (8,15,18). Epidemically or sporadically, few cases of oculoglandular tularemia have been reported in Turkey (7,10,15,19). In the present study, 2 cases conformed to the oculoglandular form and the presenting signs were ocular.

The gold standard in the diagnosis of tularemia is culture. However, culture of the bacteria requires special medium (Francis medium) and laboratory-related contamination is possible. Therefore, in addition to clinical findings, serological methods are employed for diagnosis. These include agglutination tests, immunoassay, indirect fluorescent antibody test, and Western blot, with micro-agglutination being the most common method (3,20). Agglutination at dilutions of 1/160 or more is usually considered significant, while some authors take 1/80 and over as positive (3,9,21). Especially during outbreaks, titers of ≥1/80 can be considered positive if the clinical findings are consistent with tularemia (12). Twelve of the patients included in our study were positive at dilutions of 1/160, while 3 patients were positive at 1/80.

Even if polymerase chain reaction (PCR) was not used in this study, the technic might also be used in diagnose of tularemia, and has been accepted as a very useful and confident diagnosing method frequently used in recent years. Lymph node aspirate, specimen obtained from ulcerated lesion, throat swab culture and blood are materials used in this method. PCR can be used with confidence particularly in clinically suspicious and serologically undiagnosed cases. PCR might be of benefit in patients presenting in early stages without antibody response (20).

Even if polymerase chain reaction (PCR) was not used in this study, the technique might also be used in diagnosis, of tularemia, and has been accepted as a very useful and reliable diagnosing method frequently used in recent years. Lymph node aspirate, specimens obtained from ulcerated lesions, throat swab culture, and blood are materials used in this method. PCR can be used with confidence particularly in clinically suspicious and serologically undiagnosed cases. PCR might be of benefit in patients presenting in early stages without antibody response (20).

The first choices in treatment are streptomycin and gentamicin (3). Length of treatment is 10–14 days. In recent years, quinolones, especially ciprofloxacin, have become an effective choice of treatment (3,12,14,22). Even though doxycycline can be used for treatment, it is advised that the duration of treatment is prolonged (3). Twelve cases in this study were treated with streptomycin and 3 were treated with streptomycin and doxycycline. It has been argued that starting antimicrobial treatment in the first 3 weeks of the disease is essential for complication-free outcome. However, if initiation of treatment is delayed 3 weeks, the lymph nodes could become suppurated, requiring surgical drainage (7,15). In the present study, 8 patients who started treatment early made a full recovery, whereas lymphadenopathy persisted despite antimicrobial treatment when treatment was delayed in 7 patients. These patients were followed-up by the ear, nose, and throat outpatient clinic. Mortality was not noted in any of the cases.

In conclusion, tularemia has become a leading infectious disease in response to an increase in waterborne and foodborne cases and outbreaks. Tularemia should be kept

in mind in the presence of fever unresponsive to especially beta-lactam antibiotics, membranous tonsillopharyngitis, conjunctivitis, and cervical lymphadenopathy. The most critical stage in the diagnosis is suspecting the disease. Therefore, physicians working especially in regions where the disease is frequently identified should be well informed. In regions where outbreaks are observed, making clean drinking water available and preventing the use of open waters are important in the control of the disease.

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