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Case Report

Evaluation of case series of delayed tularaemia

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ABSTRACT

Tularemia is a zoonotic disease caused by the gram-negative bacterium Francisella tularensis. Clinical suspicion is extremely important and serology is the gold standard for diagnosis. The oropharyngeal form of tularemia in Turkey takes the form of outbreaks or sporadic cases. Delay in diagnosis is the major factor in complications. Five delayed cases of tularemia in the Marmara region of Turkey are described in this paper between 2009-2015 years. All patients' diagnoses were confirmed with serology, and all had LAP on their neck regions. The lymphadenopathies persisted despite medical treatment four being excised by Ear Nose and Throat Clinic (ENT). Tularemia must be considered in the evaluation of masses on the neck, particularly in endemic areas. The most important factor in the successful management of tularemia is early initiation of treatment. The risk of suppuration and surgical interventions increases in delayed cases.

Keywords: Francisella tularensis, Lymphadenopathy, Tularemia, Endemic areas, Oropharyngeal form

INTRODUCTION

Tularemia is a zoonotic disease caused by the gram-negative coccobacillus *Francisella tularensis*. The disease is seen in the northern hemisphere and has been reported in more than 250 animal species.

Tularemia in humans can occur in several forms, including ulceroglandular, glandular, oculoglandular, pneumonic, typhoidal and oropharyngeal types.[1] The ulceroglandular and glandular forms are the most common types in the head and neck region.[2] The most common form of the disease in Turkey is the oropharyngeal form. These cases are relatively mild and derive from primary invasion of the oropharynx.[3]

The patient's clinical condition, culturing the bacteria and polymerase chain reaction are employed for diagnosis.[3,4] The other standard for diagnosis is serology. Due to the difficulty in culturing *F. tularensis*, most cases of tularemia are diagnosed on the basis of clinical picture. The detection of serum antibodies is most frequently achieved by microagglutination or tube agglutination.

Due to the prolonged course of infection, chemotherapy should be administered in order to shorten recovery time, avoid complications and reduce relapse rates. This report describes five delayed cases of tularemia from the 2009-2015 in the Marmara region of Turkey.

CASE REPORT

Informed consent forms were signed by all patients. All equipments are calibrated periodically.

Case 1: A 34 year old woman presented to our clinic with a mass on her right neck region. She reported fatigue, headache, sore throat and fever over the previous 15 days. Following these symptoms, a mass developed on her neck. Fever, pharyngitis and a 7×8 cm lymphadenopathy (LAP) were determined at clinical examination (Figure 1). Tularemia agglutination was negative in the first blood sample, but after 2 weeks the titer was 1/320 positive. The LAP developed into an abscess, and oral moxifloxacin was given for 3 weeks. Her symptoms regressed, but the LAP persisted and was eventually excised by the ear nose and throat (ENT) clinic.

Figure 1: Case 1, right neck region, 7×8 cm LAP.

Case 2: A 62-year-old man presented to our clinic with a mass on the right neck region. He reported fatigue, headache, sore throat and fever over the previous 20 days. Five days after onset of symptoms a lump developed on the right neck region. Clinical examination on presentation to our clinic revealed fever, pharyngitis and a 5×5 cm LAP (Figure 2). Tularemia agglutination titer was 1/1280 positive. The LAP developed into an abscess, and oral moxifloxacin was given for 3 weeks. His symptoms regressed, and the LAP shrank in size but persisted. It was subsequently excised by the ENT clinic.

Figure 2: Case 2, right neck region, 5×5 cm LAP.

***Case 3*:** A 53-year-old man presented to our clinic with a mass on the right neck region. He reported fatigue, sore throat and fever over the previous 20 days. At presentation to our clinic, fever and sore throat persisted and a 5×6 cm LAP was observed (Figure 3). Tularemia agglutination titer was 1/320 positive. Doxycycline was given for 2 weeks. His symptoms regressed and the LAP decreased in size but persisted. It was finally excised by the ENT clinic.

Figure 3: Case 3, right neck region, 5×6 cm LAP.

***Case 4*:** A 54-year-old woman presented to our clinic with a mass on her left neck region. She reported fatigue, sore throat, fever and the mass on her left neck region over the previous 10 days. Clinical examination revealed exudative pharyngitis and two LAPs (2×3 and 2×2 cm in size) (Figure 4). Tularemia agglutination was negative in the first blood sample, but after 2 weeks the titer was 1/160 positive. Doxycycline was given for 2 weeks. Her symptoms and LAP regressed.

Figure 4: Case 4, left neck region, 2×3 and 2×2 cm LAP.

***Case 5*:** A 61-year-old man presented to our clinic with a mass on his left neck region. Fatigue, sore throat, fever, generalized muscle pain and the mass on his right neck region had been present for 20 days. Clinical examination revealed fever and a 4×4 cm LAP on his right neck region (Figure 5). Tularemia agglutination titer was 1/1280 positive. Doxycycline was given for 2 weeks. His symptoms regressed, while LAP decreased in size but persisted. It was subsequently excised by the ENT clinic.

Figure 5: Case 5, right neck region, 4×4 cm LAP.

The characteristics of all patients are given in the Table 1.

Table 1: The characteristics of all patients.

Cases	Sex	Duration of symptoms	Agglutin-ation	Surgery
Case 1	Female	15 days	1/320 *	Excision
Case 2	Male	20 days	1/1280	Excision
Case 3	Male	20 days	1/320	Excision
Case 4	Female	10 days	1/160 *	No
Case 5	Male	20 days	1/1280	Excision

*The first blood sample is negative, the titers of two weeks later.

DISCUSSION

Tularemia is a zoonotic disease that rarely causes illness in humans. Transmission is by direct contact with infected animals, through contaminated water (most likely infected by mice) or food, by vectors or inhalation of dust or infected aerosols. The disease is not transmitted between humans.[1] The bacterium can exist for months in drinking water. Cases usually occur in fall or winter in the oropharyngeal form in Turkey. Individuals who spend time in endemic areas such as farmers, hunters, walkers and forest workers, as well as laboratory workers and veterinarians, are at high risk of tularemia.[1]

As our patients all lived in rural areas and all cases were oropharyngeal form, we attributed them to contaminated water. Before the tularemia outbreak in the region of Bursa in 1988, no cases or outbreaks had been reported in the literature in this area. The outbreak first occurred on the Bursa Karacabey Stud Farm and then spread to the South Marmara Region.[2] Due to the rarity of the disease, delays may occur in diagnosis and treatment. Epidemiological data should therefore be carefully examined. Diagnosis was delayed in our all cases. Patients presented to our clinic 10-20 days after the onset of symptoms.

Clinical suspicion is the most important factor in tularemia. After an incubation period of typically 3 to 5 days (but sometimes from 1 to 21 days), the patient experiences the sudden onset of flu-like symptoms, especially chills, fever, headache and generalized aches. Exudative pharyngitis or tonsillitis may be observed in these patients. However, enlargement of the lymph nodes is the only symptom in delayed cases.[5]

Diagnosis of human tularemia is usually confirmed by the demonstration of an antibody response to F. tularensis, which occurs approximately 10-14 days after the onset of the disease.[2] Serum antibodies are most frequently determined by microagglutination or tube agglutination.[3,5,6] Reactions at dilutions greater than 1/128 in microagglutination and 1/160 in tube agglutination are considered specific and significant for tularemia. A four-fold increase in antibody titers during illness is considered diagnostic.[5] There are some disadvantages to serological tests, such as the impossibility of determining the antibody before two weeks and cross-reactions with some other bacteria. In two of our cases, the agglutination test was negative in the first blood sample. After two weeks the titer was 1/320 (positive) in both.

The most important factor in successful treatment is to initiate medical therapy as soon as possible. Levels of suppuration and surgical interventions increase in delayed cases. Lymph node enlargement can be prevented if medical therapy is initiated in the first week.

The aminoglycosides (streptomycin and gentamicin) are the bactericidal agents used against F. tularensis and are the drugs currently employed for the treatment of tularemia infections. The fluoroquinolones, doxycycline and chloramphenicol have also been used to treat tularemia. In a recent human epidemic outbreak in Spain, the therapeutic failure rate was 23.4% for streptomycin, 4.5% for ciprofloxacin and 42.8% for doxycycline in eight-week delayed cases.[6]

CONCLUSION

The major factor that causes complication is delayed diagnosis. Our cases were delayed two or three weeks before treatment. Lymph node suppuration was present and excision was performed by the ENT clinic in four of these cases. Tularemia must not be overlooked when evaluating masses on the neck in endemic regions. The oropharyngeal form of tularemia occurs as outbreaks or sporadic cases in Turkey. Tularemia should be considered at differential diagnosis of patients with beta-lactam unresponsive tonsillopharyngitis and lymphadenopathy, especially in endemic areas. Delay in diagnosis is the major factor involved in complications.

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