

## Suppurative cervical adenopathy and pharyngeal mass due to tularemia unresponsive to medical treatment

Yasemin Özsürekci<sup>1</sup>, Mehmet Ceyhan<sup>1</sup>, Melda Çelik<sup>1</sup>, Ateş Kara<sup>1</sup>, Ali Bülent Cengiz<sup>1</sup>, Burçe Özgen-Mocan<sup>2</sup>

<sup>1</sup>Pediatric Infectious Disease Unit, Department of Pediatrics and <sup>2</sup>Department of Radiology, Hacettepe University Faculty of Medicine, Ankara, Turkey

**SUMMARY:** Özsürekci Y, Ceyhan M, Çelik M, Kara A, Cengiz AB, Özgen-Mocan B. Suppurative cervical adenopathy and pharyngeal mass due to tularemia unresponsive to medical treatment. Turk J Pediatr 2011; 53: 554-557.

Tularemia is a zoonotic disease caused by *Francisella tularensis*. Tularemia presents with various clinical forms, such as ulceroglandular, glandular, oculoglandular, oropharyngeal, pneumonic, and typhoidal tularemia forms. As an intracellular pathogen, *F. tularensis* causes granulomatous and suppurative lesions especially in the affected regional lymph nodes and various organs. Tularemia is seen most commonly in the Black Sea and Marmara regions of Turkey. Herein, we describe a girl with tularemia who presented with right cervical lymphadenopathy and left nasopharyngeal mass. To the best of our knowledge, this is the first reported case of tularemia with deep neck infection and also the first tularemia case from Corum, a city in the central Anatolian region of Turkey.

**Key words:** tularemia, deep neck infection, pediatrics.

*Francisella tularensis* (*F. tularensis*) is a small gram-negative aerobic bacilli that includes four subspecies<sup>1</sup>. Tularemia is a zoonotic disease characterized by a variety of clinical forms caused by the virulent *F. tularensis* species<sup>2</sup>. The disease may be asymptomatic, or may progress rapidly to sepsis and death if not treated properly. The major clinical forms are ulceroglandular, glandular, oculoglandular, oropharyngeal, typhoidal, and pneumonic tularemia<sup>3</sup>. Oropharyngeal infection is the most common form in Turkey and in other eastern European countries, and this has been attributed to the consumption of contaminated water and food<sup>2,4</sup>.

Herein, we describe a girl with tularemia referred to the pediatric infectious diseases clinic with right cervical lymphadenopathy and left nasopharyngeal mass. To the best of our knowledge, this is the first reported case with tularemia with deep neck infection in addition to being the first case in Corum, a city in the central Anatolian region of Turkey.

### Case Report

A 14-year-old girl with mental motor retardation was admitted due to fever and enlargement of

the right cervical lymph nodes. She did not report any tick or insect bite but came from an region endemic for Crimean Congo hemorrhagic fever. The patient was also examined for tuberculosis. The course of disease, however, clarified the diagnosis of tularemia, which was confirmed by serological tests. Serum antibody titer detected by tube agglutination test was 1/320 before treatment. Following oral doxycycline and intravenous streptomycin treatment for four weeks, the patient presented one month later with difficulty in swallowing, mass in the left nasopharyngeal area (Fig. 1) and cervical lymphadenopathy on the right side. Computed tomography (CT) revealed bilateral, ill-defined, low density collections within the deep neck tissues (Fig. 2). Intravenous ampicillin-sulbactam treatment was started with a diagnosis of deep neck infection. Real-time polymerase chain reaction (PCR) for *F. tularensis* was positive from surgical aspiration materials of the right lymph node and left nasopharyngeal mass, which was performed due to the history of tularemia. Serum agglutination test was not repeated in view of the real-time PCR positivity of the aspiration material. Pathological examination of the aspirate could



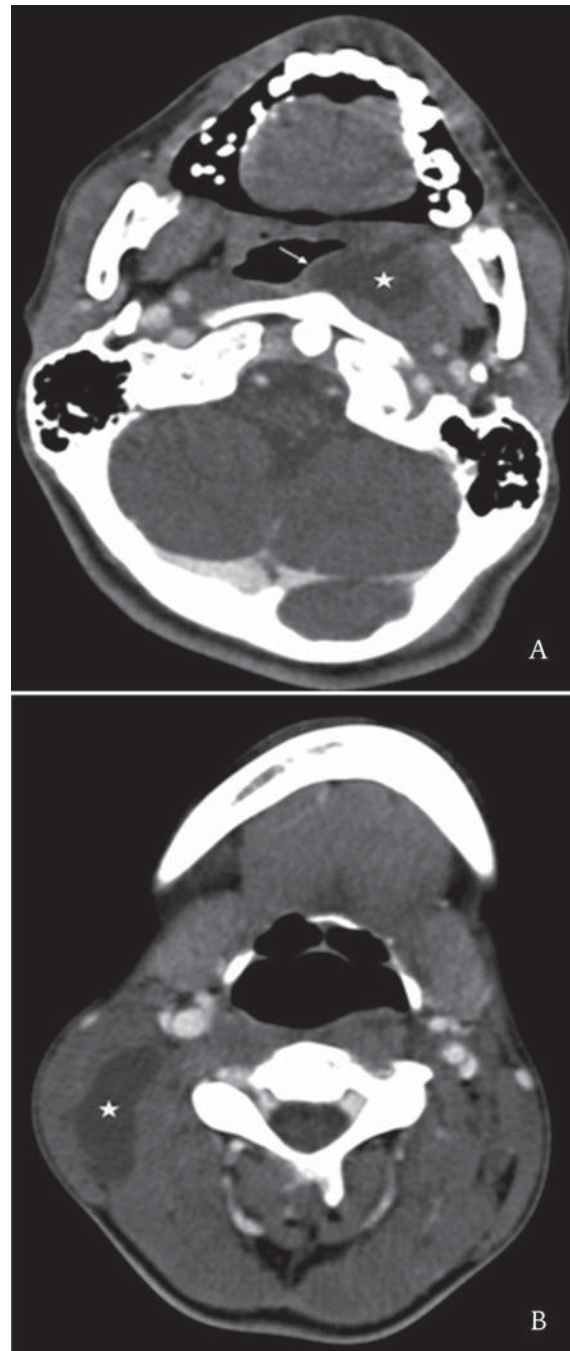
**Figure 1.** Retropharyngeal appearance of the child: (a) the left retropharyngeal swelling causing mass effect, and (b) slight narrowing of the oropharyngeal entrance.

not be done because the amount of the sample was insufficient. Therefore, the patient was retreated with doxycycline in addition to ciprofloxacin. Ciprofloxacin was changed to streptomycin due to the side effects of irritability and screaming attacks. A complete recovery was achieved after eight weeks of treatment.

#### Discussion

Tularemia is a zoonosis caused by a gram-negative, aerobic coccobacillus, *F. tularensis*. At present, there are four subspecies recognized: *F. tularensis*, *F. holarctica*, *F. mediasiatica*, and *F. novicida*. Hares, rabbits and rodents are the main animal reservoirs of the pathogen. Biting arthropods such as ticks and deerflies are important vectors. Mosquitoes have also been identified as vectors<sup>5,6</sup>. It is well known that *F. tularensis* is a highly infective bacterium, and even 10 bacteria are enough to cause the disease. The source and transmission mode of *F. tularensis* are not clear in Turkey. *F. tularensis* can be transmitted to humans by tick bites,

contact with contaminated water, handling infected materials or inhalation<sup>6,7</sup>. Our patient had no history of tick bite; however, water-borne tularemia transmission may have been the source in this patient.



**Figure 2.** Axial contrast enhanced CT of the neck revealed (a) left retropharyngeal and (b) right deep cervical collections (asterisk) with ill-defined borders. Note the mass effect on the oropharyngeal airway from the retropharyngeal lesion (arrow).

Tularemia outbreaks have been reported previously from various geographical locations in Turkey<sup>2,8-10</sup>. However, to our knowledge, this is the first report of a tularemia case from Corum in Turkey, which is an area endemic for Crimean Congo hemorrhagic fever. Perhaps this relation is not coincidental. In this region of Turkey, the most prevalent tick species are *Hyalomma*, *Rhipicephalus*, *Haemaphysalis*, *Dermacentor*, and *Ixodes*. *Ixodes* is known as the vector of both Crimean Congo hemorrhagic fever virus and *E. tularensis*<sup>7,8,11</sup>.

Tularemia usually presents with different clinical forms depending on the port of entry of the bacterium. The most common clinical form of the disease is the ulceroglandular and/or glandular form characterized by the enlargement of lymph nodes with and without an ulcer<sup>3,4</sup>. The oropharyngeal form dominates if the infection is acquired through contaminated food or water<sup>3</sup>. The oropharyngeal form of tularemia is known to be common particularly in Eastern European countries including Turkey. The clinical manifestations observed in the current case appeared similar to those of the oropharyngeal form presenting with sore throat, enlarged tonsils and mostly unilateral cervical and/or retropharyngeal lymphadenitis<sup>8,10</sup>. Our patient's first presentation was similar to the oropharyngeal form. She presented with deep neck infection in the second course without any swelling of cervical lymph nodes. Tularemia was confirmed with the real-time PCR from the surgical drainage material from the nasopharyngeal mass. To our knowledge, this is the first reported case of tularemia with deep neck infection.

The agglutination test is frequently used for the diagnosis of tularemia in the first two weeks of the disease. A single micro-agglutination titer  $\geq 160$  is considered diagnostic. This may not always be sufficient for the early diagnosis. A four-fold rise in the microagglutination titer is diagnostic for the infection. Although culture is the gold standard for the diagnosis, it is not practical due to the requirements for special media and an equipped laboratory; it also poses a significant risk of infection for laboratory personnel. PCR is useful for the diagnosis of human disease<sup>3,7</sup>.

The recommended agents for the treatment of tularemia include aminoglycosides (streptomycin or gentamicin) and tetracyclines. The fluoroquinolones are an excellent alternative<sup>9</sup>.

Sencan et al.<sup>9</sup> reported no significant differences between the different treatment protocols in the outbreak of tularemia in their region. The antibiotic choice was not a factor affecting the treatment response; however, the treatment was affected significantly by any delay in the appropriate antibiotic therapy<sup>12</sup>.

In conclusion, this report describes the first case of tularemia in middle Anatolia and also the first case of tularemia that presented as a deep neck infection. Tularemia should be kept in mind in the differential diagnosis of oropharyngeal symptoms such as deep neck infection. This case may be the first sign of tularemia outbreak in this region of Turkey, which is also an endemic region for Crimean Congo hemorrhagic fever. Further investigations are needed to determine the possible link between these two diseases and the mode of transmission in this region.

#### REFERENCES

1. Gurcan S. Francisella tularensis and tularemia in Turkey. Mikrobiyol Bul 2007; 41: 621-636.
2. Willke A, Meric M, Grunow R, et al. An outbreak of oropharyngeal tularaemia linked to natural spring water. J Med Microbiol 2009; 58: 112-116.
3. Ellis J, Oyston PCF, Gren M, Titball W. Tularemia. Clin Microbiol Rev 2002; 15: 631-646.
4. Tärnvik A, Priebe HS, Grunow R. Tularemia in Europe: an epidemiological overview. Scand J Infect Dis 2004; 36: 350-355.
5. Switaj K, Olszynska-Krowicka M, Zarnowska-Prymek H, et al. Tularaemia after tick exposure-typical presentation of rare disease misdiagnosed as atypical presentation of common diseases: a case report. Cases J 2009; 2: 7954.
6. Arikan OK, Koc C, Bozdogan O. Tularemia presenting as tonsillopharyngitis and cervical lymphadenitis: a case report and review of the literature. Eur Arch Otorhinolaryngol 2003; 260: 298-300.
7. Leblebicioglu H, Esen S, Turan D, et al. Outbreak of tularemia: a case-control study and environmental investigation in Turkey. Int J Infect Dis 2008; 12: 265-269.
8. Sahin M, Atabay HI, Bicakci Z, et al. Outbreaks of Tularemia in Turkey. Kobe J Med Sci 2007; 53: 37-42.
9. Sencan I, Sahin I, Kaya D, et al. An outbreak of oropharyngeal tularemia with cervical adenopathy predominantly in the left side. Yonsei Med J 2009; 50: 50-54.
10. Helvacı S, Gedikoglu S, Akalin H, et al. Tularaemia in Bursa, Turkey: 205 cases in 10 years. Eur J Epidemiol 2000; 16: 271-276.

11. Bursali A, Tekin S, Orhan M, Keskin A, Ozkan M. Ixodid ticks (Acari: Ixodidae) infesting humans in Tokat Province of Turkey: species diversity and seasonal activity. *J Vector Ecol* 2010; 35: 180-186.
12. Celebi G, Baruonu F, Ayoglu F, et al. Tularemia, a reemerging disease in northwest Turkey: epidemiological investigation and evaluation of treatment responses. *Jpn J Infect Dis* 2006; 59: 229-234.