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Tularemia Characterized By Cervical Lymphadenopathy in an Adolescent Child

Adolesan Bir Çocukta Servikal Lenfadenopati ile Seyreden Tularemi Olgusu

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ABSTRACT

A fifteen year old girl was consulted to us with the complaint of not getting benefit from antibiotics used to treat left oropharyngeal on going swelling lasted for seven weeks along with first two weeks of fever. Tularemia was suspected because of patient's living in rural area, being the story of drinking water from the same environment, the consistency of clinical findings and not responding to the treatment. Clinical diagnosis of tularemia was confirmed by micro agglutination testing. In conclusion, tularemia should be considered in the differential diagnosis in the patients with fever, sore throat, cervical lymphadenopathy, and particularly who do not respond to beta-lactam group antibiotics treatment.

Key Words: Tularemia, cervical lymphadenopathy, *Francisella tularensis*

ÖZET

On beş yaşında kız çocuğu, yedi haftadır devam eden sol orofarengeal şişlikle ve beraberinde ilk iki haftalık ateş nedeniyle hastanemiz dışında kullanılan antibiyotiklere cevap vermemesi üzerine tarafımıza başvurmuştur. Kırsal bölgede yaşama, aynı çevreden su içme hikâyesi olması, klinik bulguların uyumu ve tedaviye cevapsızlık olması nedeniyle tularemiden şüphelenildi. Tulareminin klinik tanısı mikroaglutinasyon testiyle doğrulandı. Sonuç olarak ateş, boğaz ağrısı, servikal lenfadenopatisi olan ve özellikle beta-laktam grubu antibiyotik tedavisine yanıt vermeyen olgularda tularemi ayırıcı tanıda dikkate alınmalıdır.

Anahtar Kelimeler: Tularemi, Servikal lenfadenopati, *Francisella tularensis*

Introduction

Francisella tularensis is a factor in gram-negative coccobacillus morphology and obligate aerobic, facultative intracellular property which causes significant infections in humans and animals. *F. tularensis* infections are seen more widely at the northern hemisphere (1). It is estimated that there are about 500,000 tularemia cases per year in the world (2). When written sources are analyzed, it is noted that tularemia cases have also increased and the infection has become an important public health problem in our country in recent years. According to the data of the Ministry of Health, although more than 1000 tularemia cases were reported in our country until 2005, the number of the cases reported between 2005-2009 after the change made in the announcement of the notifiable diseases in 2005 was reported as 1091 (3). Carrier or infected rodents play an important role in the epidemiology of the disease. Animals of this nature with secreted and extract factors can easily infect the environment and other living things. On the other hand, vectorial infection also occurs with the blood-sucking parasites. Clinical findings vary depending on the pathogenicity of the factor, the entry way to the body, the degree of systemic involvement, patient's immune efficiency, and the timely diagnosis and treatment (4). Cases of tularemia that can be seen in a wide clinical spectrum are identified at six clinical forms including ulceroglandular, oropharyngeal, oculoglandular, glandular, typhoid and pneumonia. Oropharyngeal tularemia which is seen as the most common form in our country occurs with the infection of the agent with contaminated water and food by oral route (1). The formation of cervical mass that is frequently seen at the

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oropharyngeal tularemia form is reported as a form which can be found in almost every age group and can be easily confused with other diseases; thus, the importance of taking this situation into account even in the differential diagnosis is being emphasized.

In this study, it is aimed to present a case that received clarithromycin and ceftriaxone treatment due to tonsillopharyngitis and cervical lymphadenitis in another medical center, and then, applied to our hospital for cervical mass and sore throat complaints diagnosed with oropharyngeal tularemia after detailed investigations.

Case Report

In the medical history taken, it was understood that a 15-year-old girl patient applied to another hospital with the complaints of high fever, shivering, generalized body pain and cervical mass on the left side of the neck which began about 45 days ago, received clarithromycin and ceftriaxone treatment for two weeks, but upon not benefitting from this practice, applied to our clinic. At the physical examination, while rubescent soft viscous mass, the largest with the size of 4x2 cm, at the left half of the neck was detected, hepatomegaly and splenomegaly was not detected. At the laboratory examination, white blood cell count was determined as 10200/mm^3 (62% polymorphonuclear leukocytes), hemoglobin as 13.2 mg/dL, blood platelets as 373000 (140000-400 000/mm^3), C-reactive protein (CRP) as 3.3 mg/l (0-5 mg/lt).

At the neck ultrasonography, a cystic mass at the size of 42x22 mm including internal echoes with thick and uneven at the left half of the neck was observed. At its neighborhood, the presence of a 33x17 mm second lesion with similar properties also drew attention. Neighboring soft tissues had inflammatory echogenicity-heterogeneity. Being especially more apparent on the left side, LAPs at the size of around 23x9 mm on both halves of the neck were observed.

Although the phenomena characterized with similar clinical cases do not occur frequently in the region, tularemia was suspected due to the disease's being endemic in this region, living in a rural area and in a ranching family, drinking water from the same environment and the integration of clinical findings. Positivity was detected at 1/640 titer with microagglutination test (MAT) at the serological examination conducted in microbiology laboratory for tularemia. In this case, the lack of the history of tick bite, and mouse or gnawing animal contact in this patient was found remarkable. Due to the growth of existing lymphadenopathy and aggravation of symptoms in our patient after the previous treatment, it was punctured by fine needle, and surgically treated upon the pus drainage. Drains were placed. The drain of the patient was removed at the fourth day to whom very good drainage was provided. Gentamicin 5 mg/kg/day at two doses was started to the case pre-diagnosed with oropharyngeal tularemia. Treatment was completed in 14 days and the patient was discharged. During follow-up, the fistula of the patient was observed to start to close (Figure 1).

Fig. 1. Drained LAP and closing fistula opening on the left side of the neck.

Discussion

Tularemia cases caused by *F. tularensis* attract notice as a zoonotic infection which regain importance in Turkey in recent years. It has been reported that the majority of *F. tularensis* cases in our country and in our region are emerging in winter and often in oropharyngeal form (5). The first tularemia case associated with the rabbit meat in Turkey have been reported in Tatvan where is relatively in a short distance to Van in 1938 and it was reported that tularemia epidemic which effected a total of 6 people including 5 children was associated with the ingestion of rabbit meat (6). Oropharyngeal form of the disease is stated as the most common form in our country. Differential diagnosis of ulceroglandular tularemia

cases should be made from the other infectious diseases that cause lymphadenopathy *(Staphylococcus aureus, Mycobacterium tuberculosis,* etc.), and cases such as lymphoma, head and neck malignancies, infectious mononucleosis and cat-scratch disease (7). In our case, the lack of cases with similar clinical findings and confusing with many diseases during differential diagnosis in the residence area of the patient caused a delay in the diagnosis of the disease. The disease may continue for months if left untreated. Mortality is reported to be highly reduced after the start of appropriate antibiotic treatment (7, 8). Cervical lymphadenitis which are common symptoms of the disease grow steadily when treated wrong. Untreated lymphadenitis becomes spontaneous fistula and this fistula gets closed. As in our case, beta-lactam antibiotics, macrolides, sulfonamides are ineffective drugs against tularemia agent. In our case, a broad spectrum clarithromycin and ceftriaxone treatment was not responded in another hospital.

Streptomycin and gentamicin are mostly preferred in the treatment of the disease. In recent years, the quinolone group of antibiotics has been used for treatment. Quinolons have been reported to be as successful as aminoglycosides and more successful than doxycycline in the treatment of tularemia (9). In the treatment of tularemia, fluoroquinolones may be preferred in the treatment of mild to moderate infections. In severe cases, streptomycin or gentamicin must be among alone or combined treatment options. Medical treatment is essential and early initiation of appropriate therapy is key for the success of treatment. It is recommended to do surgical drainage of the abscess cases (10). In the present case, it was determined that the patient was responsive to gentamicin (5 mg/kg/day two doses) treatment. This finding demonstrates the application of gentamicin in the treatment of severe tularemia.

Considering temporal distribution of tularemia cases, it is seen that the epidemics are examined in the transition period to the very cold seasons. Although from time to time, we see sporadic cases admitted to our clinic around Van, this case is important because of being the first case applying to our clinic from Yüksekova / Hakkari region with an altitude of 1950 m. Like most cases in the literature in terms of season, this case took place in late summer, early autumn (2,5).

Culture positivity is accepted as the "gold standard" for the definitive diagnosis of infection and it is expected to do the culture in reference laboratories with biosafety level 3. Genomic materials of F. tularensis can be detected with PCR based diagnostic methods applied to various clinical specimens in recent years. On the other hand, it is expressed in many literature that the micro-agglutination test (MAT) which has less risk of infection and is more economical, is a reliable method (5). In parallel, we applied the MAT test in our study and detected high titer antibodies. In MAT method, 1/128 titer is considered as diagnostic. *F. tularensis* antibodies remain positive in low titers for a long time (8-25 years) (3). However; if the clinical findings are consistent, 1/160 and more titers in a single measurement are considered sufficient for serological diagnosis. In this case, the titer in our patient was 1/640 and was considered very high; but because of being consistent with the clinical findings, it was accepted as sufficient for the diagnosis of tularemia. In the present case, the patient's serologic follow-up after treatment could not be done due to the regional factors such as transportation difficulties. On the other hand, serological tests required for brucellosis and syphilis for the differential diagnosis of our patients were negative. It was reported that no reproduction was detected from the abscess material taken by ENT at the first application of the patient.

As a result, it is necessary to remember tularemia and evaluate the history of the patient in detail in the differential diagnosis of LAPs which cannot be declined with beta-lactam group antibiotic treatment in endemic regions like ours. Oropharyngeal tularemia should absolutely be considered in the differential diagnosis of patients with tonsillopharyngitis resistant to penicillin treatment. It is also important to prevent the development of fistula formation by early treatment and appropriate surgical drainage.

Conflict of Interest: There is no conflict of interests between authors.

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