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Case Report

Oropharyngeal tularemia accompanied by erythema nodosum

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ABSTRACT

In recent years, there has been an increase in the reporting of tularemia cases due to factors such as rising awareness of tularemia, which is endemic in our country, or seasonal changes. Different clinical presentations of the disease may occur. One of these manifestations is erythema nodosum. In this case report, we aimed to raise awareness of this rare disease by presenting a 34-year-old female with oropharyngeal tularemia accompanied by erythema nodosum.

Keywords: Erythema nodosum, oropharyngeal tularemia, tularemia.

Erythema nodosum is characterized by erythematous, tender, nodular lesions that develop as a result of a delayed-type hypersensitivity reaction, and is most frequently seen on the extensor surfaces of the legs.[1] Septal panniculitis, which does not accompany vasculitis, is its histological finding. It can be caused by a variety of bacterial, viral, and fungal infections, with streptococcal infections being the most common. The etiologic agent, however, cannot be detected in nearly half of the cases.[1-3] Tularemia is rarely seen among infectious causes in the etiology of erythema nodosum.[3,4]

Tularemia, which is one of our country's endemic diseases, causes a zoonotic disease induced by *Francisella tularensis (F. tularensis)*, a gram-negative coccobacillus. While the consumption of non-chlorinated water or spring water is reported as a primary transmission route in our country, the most important transmission route worldwide is contact with infected animals and ticks. In previous years, especially in the Marmara Region, this disease caused epidemics, and in subsequent years, due to increased awareness or seasonal changes, it caused case reports/outbreaks in many different regions across our country.[5-14] Tularemia can be classified into six clinical forms based on the clinical involvements it causes (ulceroglandular, oropharyngeal, glandular, oculoglandular, typhoidal, and pneumonic). In the form of oropharyngeal tularemia, exudative pharyngitis/tonsillitis with symptoms such as fever, sore throat, ulcer, or lymphadenopathy may accompany this clinical picture.[4-14] It can be confused with exudative pharyngitis/tonsillitis if not treated properly.[4] However, in addition to the six classic clinical presentations, secondary skin involvement occurs at a rate of approximately 52%.[4]

We aimed to raise awareness of this rare disease in this case report by presenting a 34-year-old female with oropharyngeal tularemia accompanied by erythema nodosum.

CASE REPORT

A 34-year-old female was admitted with complaints of chills, trembling, and weakness that had lasted about 15 days. The patient's

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history revealed that swelling on the right side of the neck, cough, yellow sputum, and occasional bloody sputum had been added to these complaints for about 12 days. There were no relatives with similar complaints, but there were patients with similar complaints in their neighborhood, and the patient, almost all of whom were diagnosed with tularemia, had a history of drinking water from the common neighborhood fountain with other people diagnosed with tularemia in her neighborhood. During her physical examination, her general condition was good, she was oriented and cooperative, her body temperature was 36°C, her pulse rate was 80/min, and her blood pressure was 110/80 mmHg. The oropharynx was hyperemic, and there was a crypt within the right tonsil; there were occasional rhonchi in the lower lobe of the right lung; all other systemic examinations were normal. There was no neck lymphadenopathy. The patient was admitted to our service with a preliminary diagnosis of tularemia, serum samples were collected for serologic testing of tularemia, and empirically treatment of streptomycin intramuscular (IM) injection 1 gram 2×1 was initiated. On the second day of hospitalization, a thoracic computed tomography (CT) was performed, and no pneumonic infiltration was found. On the fourth day of her hospitalization, dermatology consultation was requested due to bilateral palpable nodular red lesions on the extensor surface of the leg, and a punch biopsy was taken from the anterior leg with the preliminary diagnosis of erythema nodosum. The patient, whose complaints and physical examination findings had regressed, was discharged on the eighth day of her treatment with a prescription for streptomycin intramuscular (IM) 1 gram 2×1 treatment for 10 days, and she was called to our outpatient clinic for follow-up. The tularemia standard tube agglutination test, which was sent on the first day of her hospitalization, was found to be negative in the outpatient clinic control, and a serum sample was sent again to make a definitive diagnosis. The tularemia standard tube agglutination test in the second serum sample was positive at a titer of 1/320, confirming the diagnosis of oropharyngeal tularemia. During the patient's subsequent follow-up, the pathologic evaluation of the punch biopsy was determined to be "septal panniculitis". A written informed consent was obtained from the patient.

DISCUSSION

Tularemia can result in a variety of secondary skin lesions.[15] Secondary skin findings were observed in 42% of tularemia cases, according to a study from Finland.[16] Erythema nodosum alone or in combination with another skin rash was the most common papular or vesiculopapular rash in 28% of patients, followed by erythema multiforme in 9% of patients. It was reported that erythema nodosum was found in 13.3% of 98 cases in our country's tularemia epidemic, which included 98 cases in Bursa.[17] Furthermore, it has been reported that erythema nodosum is more prevalent in pulmonary tularemia patients than in other types of the disease.[16] A case of oculoglandular tularemia has also been reported in the literature.[18] With this rare case report, we wanted to contribute to the scientific literature on this rare disease.

In a study of the causes of erythema nodosum in children in our country, streptococcal infection was found to be the most major cause (23%), followed by tularemia (10.2%) and tuberculosis (occult tuberculosis infection, 5%), and pulmonary tuberculosis 2.5%). In fact, four cases of dual diagnosis (streptococcal infection + *Mycoplasma pneumoniae*, streptococcal infection + occult tuberculosis infection, streptococcal infection + *Chlamydophila pneumoniae*, and tularemia + occult tuberculosis infection) have been reported.[19] In our case, the cause of erythema nodosum was tularemia infection. Two similar cases from our country have recently been reported in the literature. It was emphasized in this case report that tularemia should be considered in the differential diagnosis of exudative tonsillitis.[20]

The skin manifestations of tularemia, erythema nodosum, and erythema multiforme are thought to be the result of immune-mediated reactions.[3,16] Despite the existence of pulmonary symptoms in the presented case, no evidence of pneumonic involvement was found on radiological or physical examination.

Before diagnosing oropharyngeal tularemia in a tularemia case, ulceroglandular tularemia should be ruled out. This is due to the fact that

ulceroglandular tularemia caused by a tick or fly bite on the head and neck can induce enlarged neck lymph nodes in the absence of a primary skin ulcer. An epidemiological evaluation may be useful in identifying oropharyngeal tularemia. It is uncommon for oropharyngeal tularemia to be the primary symptom, especially when erythema nodosum persists throughout the disease. Although the cause of erythema nodosum is unknown in nearly half of cases, it is critical to identify or rule out possible infectious causes, such as tuberculosis, Valley fever, cat-scratch disease, and tularemia, as demonstrated in our presented case. Therefore, as with our patient, a comprehensive anamnesis should be performed.[4,16] Our patient had a sore throat with no accompanying lymphadenopathy. At the same time, streptococcal infection was ruled out of the patient's differential diagnosis because there was no growth of group A beta-hemolytic streptococci in the throat culture taken in the patient who had a history of using common drinking water in cases with epidemiologically similar cases. Following serological confirmation and anamnesis findings, the patient was diagnosed with oropharyngeal tularemia.

Histopathological analysis of biopsies taken from two patients in the study conducted in Bursa[17] in the patient group with erythema nodosum due to tularemia revealed dermal edema, perivascular lymphocytic infiltrate, and panniculitis. The pathologic evaluation of a punch biopsy taken from the patient in our study was also reported as “septal panniculitis”.

For the past 50 years, serological tests have been the most commonly used method for diagnosing tularemia. In addition to direct microscopic examination, bacterial production, serological tests, antigen detection, and molecular methods are used in laboratory diagnosis. Serological investigations are limited in the early disease phase because antibodies become positive after the second week and peak in the fourth-fifth weeks. Antibodies developed against the agent in the patient's serum or bacterial antigens in the acute stage can be searched serologically. The simplest diagnostic method is to look for antibodies against *F. tularensis* in agglutination tests performed in tubes or microplates. The most common method is the microagglutination test (MAT).[4,5] The diagnosis was made serologically in the case we presented, and although the initial test was negative, the test was repeated 15 days later due to high clinical suspicion, and the result was positive.

In the treatment of the disease, aminoglycosides, tetracyclines, or quinolone class antibiotics are recommended. Early treatment initiation has an impact on treatment success. Aminoglycosides (streptomycin or gentamicin) are the first choice in the treatment. Ciprofloxacin or doxycycline are recommended as alternative therapies. Because of the bactericidal action of aminoglycoside antibiotics, treatment failure and relapse are rare.[4,5] Streptomycin was used in this case, and there was no recurrence.

In conclusion, tularemia should be considered in the etiology of erythema nodosum, especially when epidemiological risk factors are present. Tularemia should be considered in the differential diagnosis of tonsillopharyngitis caused by streptococci, the most common infectious agent of erythema nodosum, and it should be remembered that they can be confused not only in terms of tonsillopharyngeal involvement but also in terms of skin findings.

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