Travel Medicine and Infectious Disease 51 (2023) 102489

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

Water-borne oculoglandular tularemia: Two complicated cases and a review of the literature

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ARTICLE INFO

Keywords:
Francisella tularensis
Oculoglandular tularemia
Oculoglandular form
Oculoglandular syndrome

ABSTRACT

Background: In this study, we presented two cases of late diagnosed complicated oculoglandular tularemia and reviewed the clinical features of oculoglandular tularemia in cases reported in the last ten years.
Method: Tularemia was diagnosed when serum microagglutination test (MAT) was ≥ 1/160 titer or when there was at least a four-fold increase in MAT titers measured over a two-week interval. We searched the oculoglandular tularemia cases reported in the last 10 years in the PubMed and Google Academic engines.
Results: Case 1 (19 M) and case 2 (15 M) had complaints of fever and burning in the eye. In both cases, the diagnosis of tularemia was delayed. Lymph node suppuration developed in both cases. A total of 19 cases of tularemia were found within the search. In the cases of oculoglandular tularemia reported in the last 10 years, submandibular and preauricular lymphadenopathy were most common after ocular findings and fever. The mean time to diagnosis was 41 ± 94 days, and the complication rate was 31.5%.
Conclusion: Tularemia should definitely be considered in cases of fever and ocular findings, especially in endemic areas. In non-endemic areas, a good anamnesis and clinical suspicion can help diagnose the disease early and reduce the complication rate.

1. Introduction

Tularemia is a zoonotic disease found in the northern hemisphere. Endemic expansion of tularemia to the southern hemisphere (especially Australia) has also been reported, where possums represent a newly described reservoir of *Francisella tularensis* [1–3]. The causative agent of the disease is *F. tularensis*, 0.2 × 0.7 μm in size, non-motile, aerobic, pleomorphic Gram-negative coccobacillus. The disease is transmitted by the human bite of arthropods or infected animals carrying *F. tularensis*, or by contact of tissue/extractions of infected animals with the skin, mucous membranes, or conjunctiva. Another transmission route of the disease is inhalation of contaminated aerosols [1,2]. Tularemia can cause epidemics by consuming contaminated water and food.

The clinical forms of tularemia differ according to the subtype of *F. tularensis*, the kind of entry routes of the bacteria and the number of inoculum, the immunity of the host, and the time of initiation of treatment. Accordingly, clinical conditions ranging from asymptomatic disease to severe illness and death can be seen. There are six clinical forms of the disease, i.e., ulceroglandular, glandular, oculoglandular, oropharyngeal, typhoidal, and pulmonary tularemia, according to the sites of involvement [2,4]. The ulceroglandular form is more common in Scandinavian countries, North America, Russia and Japan [5–8]. In Eastern European countries, including Turkey, tularemia is mostly transmitted by consuming infected water and food, and the oropharyngeal form is most common [2,8–11]. Because Tularemia can be spread through so many ways, a variety of locations are potentially at risk. *F. tularensis* is also on the list of category A biological weapons. In the case of a biological warfare attack, the pathogen could remain in the environment for extended times, potentially leading to high numbers of secondary tularemia cases. Estimated mortality rates of tularemia are various between 5% and 60% depends on the early diagnosis and appropriate treatment [12,13].

The incubation period of tularemia is 3–5 days, and the disease manifests itself with an acute flu-like picture with mostly fever, weakness, headache, sore throat symptoms. A bubonic appearance occurs in high fever and rapidly growing regional lymph node. Appropriate antibiotic treatment started in the early period alleviates symptoms and signs, and fever may persist for days in untreated cases [14]. In the oculoglandular form, when the diagnosis is delayed, complications that may require surgery such as suppuration in lymph nodes, dacryocystitis

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https://doi.org/10.1016/j.tmaid.2022.102489
Received 22 September 2022; Received in revised form 19 October 2022; Accepted 29 October 2022
Available online 5 November 2022

and nodular ulcers in the conjunctiva may occur despite treatment [14–16]. In this study, we presented two cases of late diagnosed complicated oculoglandular tularemia as a water-borne disease and reviewed the risk factors, clinical features, and clinical outcomes of oculoglandular tularemia in cases reported in the last ten years.

2. Method

Serum samples taken from the patients were sent to the Reference Laboratory for Turkey (Refik Saydam National Public Health Agency, Department of Communicable Diseases Research, National Tularemia Reference Laboratory, Ankara, Turkey). Tularemia was diagnosed when serum microagglutination test (MAT) was ≥1/160 titer or when there was at least a four-fold increase in MAT titers measured over a two-week interval.

We searched the oculoglandular tularemia cases reported in the last 10 years in the PubMed and Google Academic engines with the keywords "oculoglandular tularemia," "oculoglandular form," "francisella tularensis," and "oculoglandular syndrome." Cross-references were also included. Continuous variables were described as mean ± standard deviation (sd), while categorical variables were described as numbers and percentages.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the National Research Committee and with the ethical standards of the Declaration of Helsinki This study was approved by the Ethics Committee of Haseki Training and Research Hospital (approval number: 170–2022, date: 14.09.2022) Written informed consent were obtained from the patients.

3. Results

3.1. Cases

Case-1: A 19-year-old male patient with complaints of a sudden onset of fever, swelling under the right jaw, and pain and redness, purulent discharge in bilateral eyes. Oral amoxycillin-clavulanic acid and aminoglycoside eye drops were prescribed to the patient with the preliminary diagnosis of conjunctivitis and upper respiratory tract infection. After one week, the complaint of eye pain regressed, but the complaints of fever and painful swelling under the right jaw continued. Ampicillin-sulbactam 4 × 1 gr IV was administered to the patient, who was diagnosed with lymphadenitis at another health center, for after 14 days. The patient, whose lymphadenopathy did not regress, was referred to the Bitlis Tatvan State Hospital infectious diseases outpatient clinic. On examination, his temperature was 36.7 °C. His mouth, pharynx, and conjunctiva were normal. Painful, hard and mobile lymphadenopathy of 4 × 2 cm was detected in his right submandibular region. No pathology was detected in other system examinations. It was learned that he had been swimming in a lake before his complaints started, and that a close family member (case 2) had similar complaints. The patient was started on doxycycline 2 × 100 mg oral treatment with a preliminary diagnosis of tularemia. Simultaneously, and *F. tularensis* microagglutination test (MAT) was returned positive at 1/640 titer. The second patient, who did not use his medications regularly, appeared to the polyclinic complaining of continued swelling in the submandibular region one month later. On physical examination, fluctuation developed in the right submandibular region (Fig. 1). The patient was given a dose of 5-mg/kg per day intravenous treatment of gentamicin for 10 days. Fine-needle aspiration was performed from the relevant area three times at intervals. In the control performed three weeks later, the lymph node was found to be painless and shrunken, and there was no fluid in the fine-needle aspiration. At the end of 10 days, the patient's acute phase values and fever were within normal limits and there was no pain in the lymph node. The patient was followed up without treatment. In the follow-up one month later, it was observed that the lymph node had regressed to normal sizes.

Fig. 1. Lymphadenopathy in the right submandibular region.

Case-2: A 15-year-old male patient with complaints of fever, pain in both eyes, and painful swelling in the left jaw. He applied to the infectious diseases outpatient clinic because he had the same history as case-1, who was a family member. His temperature was measured at 37.6 °C. On physical examination, there was 3 × 1 cm painful, hard, and mobile lymphadenopathy in his left submandibular region, and hyperemia in the bilateral conjunctivae (Fig. 2). Doxycycline 2 × 100 mg tb treatment was started for the patient with a preliminary diagnosis of tularemia. Concurrently, a MAT came back negative. The patient, who did not use his medication, applied to the polyclinic again after his complaints continued one month later. On physical examination of the patient, it was observed that his left submandibular lymphadenopathy persisted. The MAT test was studied again, and it was found to be positive at 1/1280 titer. Eye examination revealed episcleritis in the bilateral conjunctiva and a 2 × 2-mm conjunctival epithelial defect in the right eye (Fig. 3). Gentamicin eye drops (4 × 2) and a 5 mg/kg intravenous treatment were administered to the patient for 10 days. In the control eye examinations performed on the fifth and tenth days of treatment, it was observed that the conjunctival epithelial defect regressed by 50%. In the third week after discharge, it was observed that the pain in the right submandibular lymph node had been resolved, but that lymphadenopathy continued and developed fluctuation. The fluctuating lesion was evacuated with fine needle aspiration. When the patient was followed up without treatment, it was found that his lymph node had regressed to normal sizes, and that the fluctuation and ocular findings had disappeared in the follow-up one month later.

3.2. Tularemia cases reported in the last 10 years

The characteristics of the tularemia cases reported in the last 10 years are shown in Table 1 [15–26]. A total of 19 cases of tularemia were

Fig. 2. Hyperemia in the bilateral region.

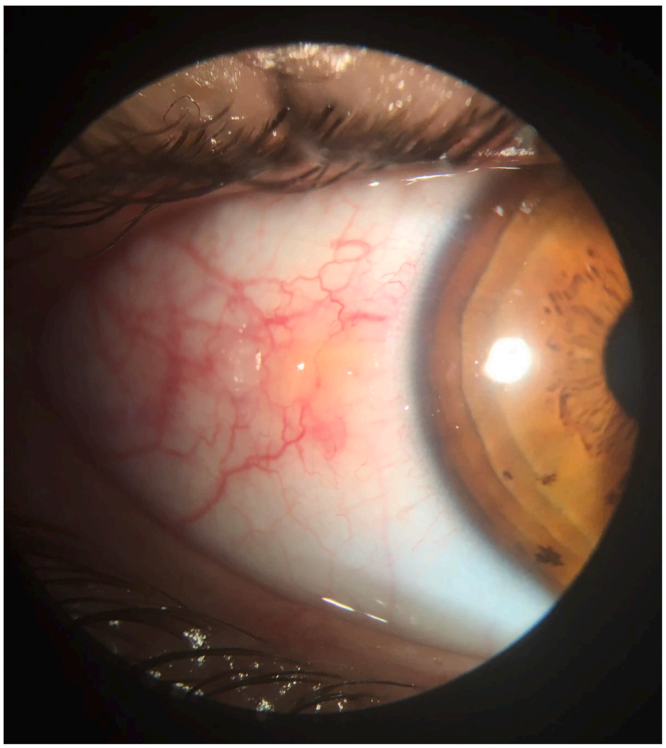

Fig. 3. Conjunctival epithelial defect accompanied by episcleritis.

found within the case, case series, and research articles. The median age of the patients was 44 (10–88) years, and 11 (61%) of the patients were male. Ten (53%) of the cases lived in an epidemic or endemic region. One of the patients had a history of visiting the epidemic area, two had a history of contact with a tick, and one had a history of contact with a rabbit. Eleven (58%) of the oculoglandular case reports were made in Turkey. When lymph node involvement was examined, it was mostly submandibular (n = 9, 47%) and preauricular (n = 9, 47%). Serological tests were mostly applied (79%) in the diagnosis of tularemia. The mean time from the onset of symptoms to diagnosis was 41 + 94 days. For the treatment of disease, streptomycin was preferred for seven patients (37%), doxycycline was preferred for five (26%), and ciprofloxacin was preferred for four (21%). Two patients refused antibiotic treatment because they were pregnant and concerned about fetal side effects. In one patient, the treatment regimen was unclear. Antibiotic-containing eye drops were used in 10 patients (53%) alongside systemic treatment. In the ciprofloxacin group (60%) followed by the aminoglycoside group (40%), eye drops were used most often in local treatment. In two patients, steroid eye drops were used in addition to systemic and local antibiotic therapy. As an eye complication, dacryocystitis was seen in one patient, and a conjunctival ulcer was seen in another. Surgical treatment was performed on five patients.

4. Discussion

This study presents two cases of complicated oculoglandular tularemia diagnosed in the infectious disease outpatient clinic of Bitlis Tatvan State Hospital. The patients resided in Hasköy district of Mus province, which is adjacent to Bitlis province. Both patients were diagnosed late and treatment was initiated late. Despite treatment, the patients took weeks to recover, and repeated lymph node aspirations were required. Ocular findings improved without sequelae.

4.1. Endemicity

Tularemia is an endemic disease in Turkey, and outbreaks have been reported in various regions [27–30]. In 2017–2019, an outbreak was reported from Mus province that coincided with the period when symptoms appeared in our cases [31]. While oculoglandular tularemia was not detected in these cases reported from Mus province, it was observed that 95% of the cases were oropharyngeal and glandular tularemia. In the same study, the author proved the cause of the epidemic to be chlorination of water, which had been neglected during infrastructure works in Bulanık district, Mus province [31]. Both cases in our article had a history of swimming in the lake in Haskoy district, Mus province, in the past. Although no outbreak was reported from Haskoy district, sporadic cases had occurred there in the past. The first and only foodborne tularemia cases reported from Turkey were from Tatvan in 1937, and no case was found thereafter [9]. Although no new cases have been reported from Tatvan, the tularemia epidemic in neighboring provinces suggests that cases may have been missed. This situation should be a warning to physicians practicing in the Tatvan region, where there is heavy patient traffic from neighboring provinces.

Ocular involvement in tularemia is rare, and symptoms usually include unilateral photophobia and conjunctival erythema [1,2,15–26]. In case 2, bilateral conjunctival erythema and edema occurred, while unilateral corneal ulceration was observed. The oculoglandular form accounts for less than 1% of tularemia cases in humans [2]. Reportedly, 3–5% of some tularemia series are oculoglandular forms [11,33,34]. However, in a multicenter study retrospectively evaluating 1036 tularemia patients, 105 (10%) cases were evaluated as oculoglandular forms [33]. The detection rate of oculoglandular tularemia was 14.5% in an epidemic in the Bala district of Ankara. In the cases of oculoglandular tularemia (n = 7, 14%) in this epidemic, fever, lymphadenopathy, periorbital edema, and chemosis were mainly observed [18]. Two of these seven patients had conjunctival epithelial defect. Similar to our case, it was observed that all these patients received local treatment in addition to systemic treatment and their ocular findings improved without sequelae [18].

4.2. Oculoglandular tularemia and different forms of tularemia

There are different clinical forms of the tularemia, i.e., ulceroglandular, glandular, oculoglandular, oropharyngeal, typhoidal, and pulmonary tularemia, depending on the portal of entry The most common form of tularemia is the ulceroglandular form, and the oropharyngeal form is more common in Turkey. Pneumonic tularemia is a more serious form with lung involvement compared to other forms. Typhoidal tularemia progresses with fever and systemic findings without localized signs of infection. It has a clinical course ranging from acute sepsis to chronic febrile condition. It is also called abdominal tularemia because of the predominant complaint of abdominal pain. Pulmonary involvement secondary to hematogenous spread may be seen [1,2,4].

We reviewed oculoglandular form in this study. There are a limited number of case reports of oculoglandular tularemia in the literature (Table). Dacryocystitis and nodular ulcers are rare complications of oculoglandular tulemia requiring surgery [15,16]. It has been observed that complicated cases are often characterized by late diagnosis of tularemia. One case was a 27-year-old pregnant woman who was hospitalized after the onset of her symptoms and was not given effective antibiotics for tularemia the first time. After diagnosis, the patient refused systemic antibiotic therapy because of the effects on the fetus, so repeated surgical drainage was performed when the disease recurred. In this case, a ciprofloxacin-absorbed sponge was placed on the tissue defect area because of the recurrence. The patient has had no recurrence for six months [15]. Another patient is a 44-year-old case reported from Germany. After a visit to the endemic area, the patient complained of headache and swollen eyelids, and because he did not respond to empiric treatment with co-amoxicillin, he was referred for further treatment. Ocular examination revealed conjunctival ulceration, and it was reported that the cervical lymphadenopathies had progressed under intensive antibiotic treatment, the lymphoid ganglia had to be surgically

Table 1
Clinical features of oculoglandular tularemia cases reported in the last 10 years.

Reference/year	Sources/risks	Age/ Gender	Symptoms/signs	Time to diagnosis	Diagnostic method	Treatment/duration (days)	Complications
Celik T, 2014 [15]	Living in an epidemic zone	27/F(18 W pregnant)	Fever (37.5 °C), headache, malaise, purulent conjunctivitis, preauricular and submandibular lymphadenopathy	21 days	Serology	Gentamicin eye drops 7 days Plus sponge impregnated with ciprofloxacin	Surgical drainage and debridement for Dacryocystitis, fluctuation in lymph ganglion
Zamboni SL, 2012 [16]	Farmer, rabbit hunting	68/NA	Fever (39.7 °C), Cough, left ear pain, preauricular and cervical lymphadenopathy, belapharitis	NA	NA (Swab of ulcer)	Doxycycline 2 × 100 mg 14 days	–
	Visit the endemic area	44/M	Fever, headache, eyelid swelling, follicular conjunctivitis, conjunctival ulcer, submandibular lymphadenopathy	NA	NA (Lymph node)	Erythromycin, gentamicin, clindamycin, doxycycline, ciprofloxacin about 7–10 days	Partial improvement in eye findings Surgical lmph node excision
Eren Gok S, 2014 [17]	Living in an epidemic zone	65/F	Fever (37.8 °C), Preauricular lymphadenopathy, Episcleritis	7 days	Serology	Ciprofloxacin 2 × 400 mg IV 7 days then 2x500 orally 14 days Plus Ciprofloxacin eye drops 7 days	–
	Living in an epidemic zone	34/M	Fever (38.7 °C), Jugular left lymphadenopaty, Periorbital edema, follicular conjunctivitis, conjunctival epithelial defects, Secretion	3 days	Serology	Streptomycin 2x1gr 3days then 1x1gr 11 days Plus Ciprofloxacin eye drops (7)	–
	Living in an epidemic zone	49/M	Fever (39 °C), preauricular and submandibular lymphadenopathy, Periorbital edema, follicular conjunctivitis conjunctival epithelial defects	3 days	Serology	Streptomycin 2x1gr 3days then 1x1gr 11 days Plus Ciprofloxacin eye drops (7)	–
	Living in an epidemic zone	78/M	Fever (39 °C), swelling Left parotis, Periorbital edema and hyperemia	21 days	Serology	Ciprofloxacin 2 × 400 mg IV 7 days then 2x500 orally 14 days Plus Ciprofloxacin eye drops (7)	–
	Living in an epidemic zone	64/F	Fever (37 °C), preauricular and retroauricular lymphadenopathy, Periorbital edema, konjunctivitis	4 days	Serology	Streptomycin 2x1gr 3 days then 1x1gr 11days Plus Tobramycineeye drops (7) Plus Oinment eye drops (7)	–
	Living in an epidemic zone	60/M	Fever (39 °C), preauricular and submandibular lymphadenopathy. Periorbital edema, Ptosis in left eye, chemosis, purulent secretion, conjunctival hyperemia	2 days	Serology	Streptomycin 2x1gr 3 days then 1x1gr 11days Plus Tobramycineeye drops (7) Plus Oinment eye drops (7)	–
	Living in an epidemic zone	41/M	Submandibular lymphadenopathy. Periorbital edema and hyperemia	3 days	Serology	Streptomycin 2x1gr 3 days then 1x1gr 7 days Doxycycline 2 × 100 mg 10 days Plus Ciprofloxacin eye drops 7 days	–
Lakos A, 2020 [18]	Tick-born	25/M	Fever, Periorbital edema, purulent discharge from the conjunctiva, lacrimation, preauricular lymphadenopathy	4 days	Serology	Doxycycline 2 × 100 mg 20 days Plus Tobramycine eye drops 7 days	–
Kreutzmann T, 2021 [19]	NA	60/M	Fever (39.5 °C), Chemosis, diplopia, decreased vision, orbital cellulitis and preauricular lymph node swelling, Abscess in the parotid gland	33 days	Serology PCR (Blood)	Ciprofloxacin 2 × 400 mg 7 days later changed to doxycycline 7 days due to side effects	Parotid abscess incision Surgical lmph node excision
Altuntas EE, 2012 [20]	Living in an endemic zone	18/F	Left submandibular lymphadenopathy, ecchymosis around the eyes and redness of the eye	NA	Serology	Doxycycline 2 × 100 mg 21 days	–
Kosker M, 2013 [21]	Living in an endemic zone	15/M	Hyperemia, crusting on eyelesh and swelling, submandibular	30 days	PCR (needle apriate from	Gentamisin 5 mg/kg 1x1 14 days	Surgical lmph node excision

(*continued on next page*)

Table 1 (*continued*)

Reference/year	Sources/risks	Age/ Gender	Symptoms/signs	Time to diagnosis	Diagnostic method	Treatment/duration (days)	Complications
			swelling, conglomerated lymphadenopathy		preauricular mass)	Later changed to streptomisin 1x1 gr 10 days Plus Tetracycline 56 days	
Frischknecht M, 2019 [22]	Direct inoculation contominated oil	13/F	Fever, sore throat, reddened eye, swollen eyelid, papiler conjunctivitis, submandibular lymphadenomegaly	NA	Culture and PCR (conjunctival swab)	Ciprofloxacin 2 × 500 mg 14 days Plus Ofloxacin eye drops Plus polymyxin/neomisin eye drops	–
Terrada C, 2016 [23]	Rabbit	52/M	Fever, headache, bilateral uveitis, subretinal hemorrhage, Choroidal granuloma	1 year	Serology	Doxycycline 2 × 100 mg 21 days	–
Rastawicki W, 2020 [24]	Tick-born	10/F	Fever, swollen eyelid of the right eye, erythema of the right cheek and conjunctivit	18 days	Serology	Doxycycline 2 × 100 mg (NA)	Fluctuation in lymph ganglion
Donate-Pérez-Molino, 2018 [25]	NA	88/M	Pain and discharge in the right eye, cervical mass, intraparotid lymphadenopathy	60 days	Serology PCR (Lymph node)	Streptomycin 2x10 mg/ kg 14 days	–
Celik T, 2014 [26]	NA	18/F (16 W pregnant)	Fever (38 °C), swelling and reddnes neck, puffy eyelids, pseudoptosis, preauricular and submandibular lymphadenopathy	NA	Serology PCR (abscess)	Cefuroxime 2x500 42 days (refused to aminoglycosid/ quinolane cause of side effects on fetus)	Surgical drenaj on absess

NA: not available, F: female, M: male, W: weeks, PCR: polymerase chain reaction.

removed, and the patient's ocular symptoms regressed [16]. Of two oculoglandular patients with atypical findings, one presented with conjunctivitis with swelling in the left corner of the lip, the other with fever, and the other with bilateral conjunctivitis and erythematous multiform rash on the hands and arms [35]. As the cases show, the diagnosis of tularemia is made late because the disease presents with various interrelated clinical symptoms and is not suspected from the beginning. The time from onset of symptoms to diagnosis in tularemia patients has been reported to be 21 days or more [14,18,30,32,33]. In our two cases, the diagnosis time was also 21 days. In a study of oculoglandular tularemia cases reported over the past decade, the mean diagnosis time was 41 days and the complication rate was 31.5% (Table 1). In a study evaluating 205 cases in Turkey, the complication rate was 40% in cases in which the time from symptom onset to diagnosis was more than 21 days [27]. Researchers have emphasized that treatment success does not depend on ineffective antibiotics and the antibiotic itself, but that the timing of treatment initiation is important [27,36,37].

4.3. Modes of transmission

The oropharyngeal form of tularemia is the most common in Turkey. Transmission to humans usually occurs through oral ingestion of water and/or food contaminated with rodents. The most likely route of oculoglandular tularemia transmission is inoculating the bacteria with *F. tularencis* through direct contact of contaminated water with the conjunctiva [2,9,18]. Tularemia may be spread through inhalation of dried animal matter, skinning or dressing killed animals, or drinking water contaminated by animal carcasses.

4.4. Affected populations/outdoor exposure opportunities

The visitors and campers to rural areas and those in contact with water in canals, lakes, ponds, streams and rivers may be exposed to the infection lead to increased risk to exposure to the bacterium that causes tularemia. The risk may be greater for those who swim canoe, kayak, wade or participate in other water activities in contaminated water like our cases. In 2000, an outbreak of pulmonary tularemia was reported in Martha's Vineyard, a touristic island in the United States [38,39]. There are also cases of airway-induced tularemia reported in farmers [40]. So those who are interested in agricultural tourism and those who visit touristic places where the pneumonic tularemia epidemic have risk to transmission of tularemia. In this review artropad bite and animal contact, living and travelling to endemic region were transmissions routes of oculaglanduler tularemia. However, there were no confirmed cases of aerosolised transmission among oculoglandülar tularemia cases. In order to protect travelers from tularmia, it is recommended to use insect repellent containing DEET on their skin, or treat clothing with repellent containing permethrin, to prevent insect bites. In addition it should be suggest that wash their hands often, using soap and warm water, especially after handling animal carcasses, be sure to cook their food thoroughly and that their water is from a safe source [41,42].

4.5. Diagnostic tests

Serological tests are most commonly used to diagnose tularemia. Although cultural positivity is the most sensitive method, it is not used as a routine diagnostic test because of disadvantages such as high contagiosity, hazards to laboratory personnel, and the need for special reproduction media [1,2,9,14]. The most commonly used serological test is the MAT test. It takes two weeks for antibodies to reach their highest concentration in tularemia. Therefore, an early MAT test may be negative or positive with a low titer. In suspected cases, a control MAT test should be requested two weeks later [1,9,14]. PCR testing is another diagnostic method [1,43,44]. PCR of *F. tularensis* was positive in specimens from the lymph nodes of two of the four patients with Perinaud's syndrome, from the surgically removed nodular ulcer of one patient, and from the eye swab of the other patient. The authors emphasized that PCR testing may be a good alternative to cultures and late-positive serological tests in the diagnosis of rare oculoglandular tularemia [44]. Histopathological examination is one of the auxiliary methods in diagnosis [1,2,9]. However, the chronic caseating granulomatous inflammation that usually occurs in tularemia may lead to the misdiagnosis of tuberculosis. Even in cases with negative tuberculosis culture, tests should be requested to diagnose tularemia and should be investigated for granulomatous lymphadenitis [30,45,46]. In addition to tuberculosis, other

infectious agents that can cause granulomatous inflammation (i.e., streptococcal or staphylococcal lymphadenitis, cat scratch disease, sporotrichosis, toxoplasmosis, fungal or atypical mycobacterial infections, rat-bite fever, anthrax, plague, syphilis, and other sexually transmitted infections) should be considered [1].

4.6. Treatment options

The first recommended options for the treatment of tularemia are streptomycin and gentamicin [1,2,15]. Doxycycline is an alternative antibiotic that allows outpatient treatment of tularemia patients through oral administration. Because it is bacteriostatic, the recommended duration of treatment is longer. On the other hand, ciprofloxacin is an agent with high treatment success that can be preferred in severe patients and in outpatients with oral and intravenous administration. Although treatment of tularemia in pregnant women is controversial, gentamicin and ciprofloxacin are recommended [2]. Although no treatment different from other forms of tularemia is recommended for the treatment of oculoglandular tularemia, gentamicin and ciprofloxacin eye drops have been commonly used in cases (Table 1). However, there is no study on oculoglandular tularemia and local treatment. It has been suggested that one of the reasons for local treatment of patients with ocular findings may be that it was started before diagnosis or that their coinfections could not be excluded.

4.7. Limitations

In this study, we presented two cases of oculoglandular tularemia which is a rare form. In addition, we examined oculoglandular tularemia cases in the last decade. Serum MAT test and ocular findings were used in the diagnosis of oculoglandular tularemia, since culture and PCR testing could not be performed due to shortcomings of our laboratory (i.e., PCR testing and biosafety level capacity). Although this seems to be a limitation of this study, it has been observed that the lesions in the eyes regressed with appropriate treatment. In most reports in the literature, serum MAT was used for the diagnosis. Another limitation is that some cases may be missed in search results/engines.

5. Conclusion

Tularemia should definitely be considered as differential diagnosis in cases of nonspecific fever, lymphadenopathy and ocular findings, especially in endemic and newly emerging endemic regions. In non-endemic areas, a good medical history for travelling endemic regions or vector contact, and clinical suspicion can help diagnose the disease early and reduce the complication rate. Raising awareness of tularaemia among particular risk groups, such as travelers is crucial. The nonspecific signs of tularemia complicate the diagnosis for medical practitioners and can contribute to underreporting. To avoid misdiagnosis of oculoglandular tularemia, ophthalmologists, family physicians, and otolaryngologists should be educated about tularemia in addition to infectious diseases specialists.

CRediT authorship contribution statement

Betul Copur: designed the study, wrote the protocol, and managed the study, performed the statistics, interpreted the data, and, Writing – original draft, were involved in collecting the data, a critical review of the manuscript, All authors provided inputs for revision of the manuscript, communicated with the journal and addressed comments from reviewers, Funding acquisition, Formal analysis, data interpretation, Writing – review & editing. **Serkan Surme:** designed the study, wrote the protocol, and managed the study, were involved in collecting the data, a critical review of the manuscript, All authors provided inputs for revision of the manuscript, Funding acquisition, Formal analysis, data interpretation, Writing – review & editing.

Declaration of competing interest

The authors declare no competing interests.

Acknowledgements

We would like to thank all, Dr. Selçuk Kılıç who studied the serum MAT test in the National Reference and Diagnosis Center, our fellow physicians who worked in the Ear-Nose-Throat Clinic of Bitlis Tatvan State Hospital in 2018, who provided intermittent fine needle drainage support, and Dr. Mehmet Dusunur for their help in the eye examination.

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