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Ocular Manifestations of Tularemia

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Abstract

Tularemia is a bacterial zoonozis caused by *Francisella tularensis*, a highly virulent, aerobic, intracellular gram-negative coccobacillus. Since oculoglandular form is one of the rarest forms the disease, ocular manifestations of tularemia are mostly as case reports and small case series in literature. Ophthalmologists should be aware of ocular manifestations of this disease because early diagnosis is important for resolving the infection and preventing the complications. In this report, we evaluate the clinical features of tularemia patients, focusing on the ocular signs and review the literature with reported ophthalmic findings.

Keywords: *Francisella tularensis*; Tularemia; Oculoglandular tularemia; Parinaud's syndrome

Introduction

Tularemia is a bacterial zoonozis caused by *Francisella tularensis*, a highly virulent, aerobic, intracellular gram-negative coccobacillus. *F. tularensis* is predominant in the northern hemisphere, especially in Russia, Kazakhstan, Turkmenistan, North America, Canada, Japan and Scandinavian countries such as Finland and Sweden [1]. Additionally, tularemia cases have been reported from Australia, Spain, Kosovo, Switzerland, and Turkey [1-4]. Tularemia has been identified in a variety of mammalian species and wild animals such as raccoons, cats, dogs, and cattles, humans, hares and rodents [5].Transmission of *F. tularensis* to humans may be *via* insect bites, contact of the skin or mucosa with infected tissue, inhalation of the bacteriaor infecting particles, or consumption of contaminated water or food. After exposure, symptoms appear an incubation period of between 1 and 14 days (usually 3-6 days) [6,7]. The purpose of this report is to evaluate the clinical features of tularemia patients, focusing on the ocular form and review the literature with reported ophthalmic findings.

About Tularemia

Six major clinical subtypes have been defined depending on the route of entry: ulceroglandular, glandular, pneumonic, typhoidal, oculoglandular, and oropharyngeal tularemia. The most frequently encountered subtype of tularemia is the ulceroglandular form, involving a skin ulcer at the point of contact and painful regional lymphadenopathy associated with withacute onset symptoms of fever, headache, myalgia, arthralgia, fatigue, vomiting and diarrhea and usually occurs following an insect bite or handing of an infected animal after an incubation period of 3-6 days [6-8].

In Eastern European region and Turkeythe most common clinical presentation of tularemia is the oropharyngeal form caused by the consumption of contaminated water and foodwith clinical signs of sore throat, fever, and neck mass [9]. Previously, we have reported a patient who developed nasolacrimal duct obstruction and dacryocystitis associated with oropharyngeal tularemia [10]. In this case, we hypothesized that the tularemia infection and local inflammation cause edema in the mucous membranes, fibrosis formation in the nasolacrimal duct and subsequently recurrent episodes of dacryocystitis.

Oculoglandular tularemia is one of the rarest seen, comprising up to 3%–5% of all cases [1,5]. Transmission of oculoglandular form is thought to be through direct contact with infected materials, often *via* eye rubbing with contaminated fingers, or contact with contaminated particles, aerosols and fluids [11]. This form of disease, also known as Parinaudoculoglandular syndrome, is a conjunctival disease characterized by unilateral painful, purulent, granulomatous conjunctivitis associated with homolateral preauricular, submandibular, cervical, parotid, or axillary lymphadenopaty, and systemic symptoms such as headaches, anorexia, fever and sore throat [12]. Patients present with varied ocular symptoms, which may include mucopurulent discharge, conjunctival chemosis, epithelial defects, ulceration, nodules, periorbital edema and less commonly corneal ulcer. In a prospective study, Eren Gok et al. evaluated the tularemia patients during an outbreak. They reported the rate of oculoglandular tularemia was 14.58% (7/48), presented with follicular conjunctivitis and conjunctival epithelial defects [13]. Parinaudoculoglandular syndrome has been associated with several infectious diseases including Bartonellahenselae (cat-scratch disease), Mycobacterium tuberculosis, Sporotrichosis, Chlamydia trachomatis, Herpes infections and tularemia which is rarely considered in the differential diagnosis. Oculoglandular tularemia can involve the eyes, eyelids, and more rarely, the lacrimal system [11,14,15]. Çelik et al. reported a lacrimal system involvement in oculoglandular tularemia, as purulent conjunctivitis and acute dacryocystitis with a large abscess in a 27-year-old woman who was 18 weeks gestation [16]. Patient was treated with topical gentamicin and oral amoxicillin-clavulanic acid therapy for 2 weeks because of the pregnancy, and surgical drainage for dacryocystitis subsequently.

Parinaud'soculoglandular syndrome has been the most common ophthalmologic complication reported in the course of tularemia [12]. However, a few different ocular manifestations in the course of tularemia have also been reported in the literature. Terrada et al. reported a case of posterior uveitis as an infrequent manifestation of tularemia infection [17]. One case of serpiginous like choroiditis, atypical variant of usual presentation, has also been reported [18].

Additionally, there is a unique case of oculoglandular Parinaud syndrome presenting with acute angle-closure glaucoma and corneal edema in the literature [19].

Diagnosis of tularemia is based on combination of clinical findings and serological tests. Culture isolation is difficult because of the small colonies, weakly Gram staining of *F. tularensis* and low isolation rate from conjuctival swab material (5%) [20]. In addition, to natural ocurrence of bactery, *F. tularensis* considered as a potential bioterrorism agent and requires special biosafety conditions. Several serology methods such as enzyme-linked immunosorbent assay (ELISA), microagglutination, hemagglutination and tube agglutination are most commonly used in clinical practice for diagnosis. A positive serologic result was defined as a single antibody titreof 1/160 or greater in the serum sample and considered diagnostic for tularemia [21]. Newer methods to confirm the bactery presence include direct fluorescent antibody staining, urine antigen detection, polymerase chain reaction (PCR) and RNA hybridization. Polymerase chain reaction (PCR) assays, have a high sensitivity and specifity in determining *F. tularensis* DNA in blood serum or swap sample of patients and it is a very useful alternative for early confirmation of clinical diagnosis [20-22].

The first line agents recommended for general treatment are antibiotics such as gentamycin or streptomycin for 10 days; doxycycline or ciprofloxacin as an alternative choice for patients who cannot to larateaminoglicosides [23].Topical treatment options are ciprofloxacin and tobramycin ophthalmic drops and or tobramycin ointment for 2-3 weeks [13]. Kosker et al. reported a patient with oculoglandular tularemia non-responsive to gentamicin and needed for long-term antimicrobial treatment and lymph node excision subsequently [24].

Conclusion

Physicians should be aware of tularemia, particularly in endemic countries, when a patient develops fever, pharyngitis, cervical lymphadenopathy or conjunctivitis non-responsive to beta-lactam antibiotics. Moreover, oculoglandular tularemia is not only suspected in cases who complain of systemic symptoms and purulent conjunctivitis; it should also be suspected in patients admitted to the hospital with corneal ulcer, acute dacryocystitis, uveitis or choroiditis in areas where *F. tularensis* is prevalent. As the ocular forms are extremely rare and the overall index of suspicion is low, ophthalmologists should be aware of the ruling out an infectious origin in endemic areas. The early administration of appropriate treatment and follow-up of the patient is important to resolve the infection and prevent the complications caused by this disease.

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