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Ocular Brucellosis: Case Report and Literature Review

Oküler Bruselloz: Olgu Sunumu ve Literatür Derlemesi

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Abstract

Brucellosis is a systemic zoonotic infection transmitted to humans by contact with the body fluids of infected animals or consumption of infected animal products. Although nearly eradicated in many developed countries, the disease is still endemic in Middle and South America, Central Asia, the Arabian Peninsula, Middle East, and Mediterranean regions. Any organ or system of the body may be involved. Skeletal system, spleen, liver, and bone marrow are the most frequently affected sites. Ocular involvement is reported relatively rarely, in 3.4%–26% of brucellosis cases, usually as a complication of chronic phases of the disease. Although ocular complications have been known since the early 20th century, decades after recognition of the disease, there is no convincing data about its true incidence, as most citations in the literature refer to case reports. Ocular brucellosis has severe complications and may result in total loss of vision in a quarter of patients despite appropriate treatment. A literature search conducted in PubMed on 10 September 2018 using the keywords "ocular-brucellosis" and "uveitis-brucellosis" and limiting to only human studies in the English literature published after 1950 yielded 27 and 29 articles, respectively. Of these, 14 were case reports or case series and included a total of 131 cases. We also found five case reports by searching for "oküler-brusella" and "göz-brusella", two in the Turkish Medline database (www.turkmedline.net) and four in Google search, with a total of six cases. Herein, we describe a case of ocular involvement of chronic brucellosis presenting with chorioretinitis that led to severe visual loss, and present a systematic review of previous cases reports and series in the literature. We believe that in an endemic area such as our country, routine ophthalmologic evaluation of all patients diagnosed with brucellosis and immediate initiation of therapy are necessary to prevent disease progression and severe sequelae.

Keywords: Glaucoma, dacryoadenitis, ocular involvement, ophthalmologic, optic neuritis

Öz

Bruselloz sistemik bir zoonotik hastalık olup, insana enfekte hayvanın vücut sıvıları ile temasla veya bu hayvanların ürünlerinin tüketilmesi ile bulaşır. Birçok gelişmiş ülkede eradike edilmiş olmakla birlikte halen Orta ve Güney Amerika, Orta Asya, Arap Körfezi, Orta Doğu ve Akdeniz Bölgesi'nde endemiktir. Vücuttaki her sistem ve organ etkilenebilir. Kas ve iskelet sistemi, dalak, karaciğer ve kemik iliği en sık tutulan bölgelerdir. Oküler tutulum daha nadir olarak, çeşitli yayınlarda %3,4 ile %26 arasında ve çoğunlukla hastalığın kronik formunda bildirilmiştir. Göz komplikasyonları hastalığın tanımlanmasından on yıllar sonra, 20. yüzyılın başından beri tanımlanmakla birlikte gerçek insidans mevcut literatürün olgu sunumlarından ibaret olmasından dolayı bilinmemektedir. Oküler bruselloz ciddi komplikasyonlar ile seyredebilmekte ve uygun tedaviye rağmen hastaların dörtte birinde görme kaybı ile sonuçlanabilmektedir. Konuyla ilgili 10 Eylül 2018 tarihinde PubMed'de "ocular-brucellosis" ve "uveitis-brucellosis" anahtar kelimeleri ile tarama yapıldığında ve tarama İngilizce literatür, insan çalışmaları ve 1950 sonrası basılması ile sınırlandırıldığında sırasıyla 27 ve 29 çalışma bulunmuş, çalışmalar incelendiğinde toplamda 131 olgu içeren 14 olgu ve olgu serisi sunulduğu görülmüştür. Ayrıca Türkçe yayınlar incelendiğinde "oküler-brusella" ve "göz-brusella" anahtar kelimeleri ile: "Türk Medline" (www.turkmedline.net) da iki ve Google search ayrıca üç olmak üzere altı olgu içeren beş makale bulunmuştur. Bu yazıda koryoretinit ile gelen, tedaviye rağmen

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Öz

ciddi görme kaybı ile sonuçlanan bir oküler brusella olgusu sunulmuş ve ilgili literatür olgu sunumları/serilerin sistematik derlemesi yapılmıştır. Bu veriler ışığında ülkemiz gibi brusellozun endemik olduğu bölgelerde hastalığın ilerlemesini ve komplikasyonlarını önlemek açısından bruselloz teşhisi konulan her hastaya göz muayenesi yapılması, erken tanı ve hızlı tedavi başlanması gerekliliği vurgulanmıştır.

Anahtar Kelimeler: Glokom, dakriyoadenit, göz tutulumu, oftalmolojik, optik nörit

Introduction

Brucellosis is a systemic zoonotic infection present worldwide. It is transmitted to humans by contact with body fluids of infected animals or consumption of infected animal products. Although nearly eradicated in developed countries due to proper livestock vaccination and control of food of animal origin, the disease is still endemic in the Mediterranean region, in which Turkey is also located^[1,2]. Among the six pathogenic species in the genus, four have been recognized as human pathogens: Brucella abortus, Brucella canis, Brucella suis, and the most virulent, Brucella melitensis, which is isolated in most of the cases in Turkey^[1,2]. Any organ or system of the body can be involved, with skeletal system, spleen, liver, and bone marrow being the most frequently affected sites^[1]. Ocular involvement is relatively rare, reported in 3.4-26% of cases, and is usually a complication of chronic phases of the disease^[3-7]. Ocular brucellosis most commonly presents with uveitis; other manifestations include keratoconjunctivitis, corneal ulcers, iridocyclitis, nummular keratitis, choroiditis, optic neuritis, papilledema, and endophthalmitis^[3]. The disease has severe complications and may result in total loss of vision in a quarter of patients despite appropriate treatment^[3]. Herein, we describe a case of ocular involvement of chronic brucellosis presenting with chorioretinitis that led to severe visual loss, and present a systematic review of previous cases reports and series in the literature.

Case Report

A 36-year-old female was referred with a two-month history of severe decrease in visual acuity in the right eye. Fundoscopic examination revealed posterior uveitis with chorioretinitis (Figure 1). Possible etiologies were investigated by taking a detailed history and performing laboratory tests. All autoimmune markers as well as infectious serology (herpes simplex virus, cytomegalovirus, syphilis, toxoplasmosis, hepatitis B surface antigen, anti-hepatitis C virus, anti-Human Immunodeficiency Virus) were negative except for positive Rose-Bengal and serum *Brucella* standard tube agglutination (STA) tests (1/320) (ODAK Diagnostics, İstanbul, Turkey). The patient had a history of unpasteurized milk product consumption but no other signs or symptoms related to brucellosis. She had no systemic complaints or signs of other organ involvement. Laboratory values were all normal, with blood glucose: 87 mg/dl, aspartate aminotransferase: 17 u/l, alanine aminotransferase: 16 u/l, blood urea nitrogen: 33 mg/dl, creatinin: 0.6 mg/dl, and serum C-reactive protein level: 0.8 mg/l, erythrocyte sedimentation rate: 20 mm/h, and normal complete blood count with white blood cells: 4950/mm³ and platelet count: 255,000/mm³. The patient was diagnosed with brucellosis with ocular involvement. Visual acuity in the right eye was severely impaired with 95% visual loss at the start of treatment. She was started on oral doxycycline 100 mg twice daily and rifampicin 600 mg/day along with topical steroids and a nonsteroidal anti-inflammatory drug. At the end of six weeks of treatment, she had no visual improvement despite some reduction of inflammation observed on fundoscopic examination, and intramuscular streptomycin 1 g/day was added to therapy for two weeks. The patient's visual acuity remained at counting fingers after eight weeks of treatment and at four-month follow-up, and STA was positive with a titer of 1/160.

Literature Review

Herein, we reported a case of ocular involvement of chronic brucellosis presented with chorioretinitis. A literature search in PubMed on 10 September 2018 using the keywords "ocularbrucellosis" and "uveitis-brucellosis" yielded 58 and 59 articles,



Figure 1. Ocular involvement of Brucella: severe chorioretinitis

respectively. Constricting the search to only human studies reduced these numbers to 45 and 50, respectively. After filtering the results for those in the English literature, 27 and 29 articles remained. Of these, a total of 14 were case reports or case series and included a total of 131 cases. A flow diagram presenting the number of studies screened, assessed for eligibility, and included in the review is shown in Algorithm 1. We also found five case reports by searching for "oküler-brusella" and "göz-brusella", two in the Turkish Medline database (www.turkmedline.net) and four in Google search, with a total of six cases.

Historically, brucellosis was first recognized in the Mediterranean region, particularly in goats and sheep, dating back to antiquity. Centuries later, a British physician named David Bruce first isolated the causative organism from four fatal cases in 1887 and named the disease Micrococcus melitensis. A few decades later in 1924, Lemaire^[8] described the first case of ocular involvement, a case of bilateral optic neuritis in a patient with acute brucellosis. In 1951, Pagliarani^[9] published a study entitled "Contribution to the knowledge of ocular manifestations due to Brucella infection in man" in which he stated that "in these circumstances the diagnosis is less easily done and this fact makes us to believe that the incidence of ocular manifestations is more frequent than the perusal of the literature would suggest". Since then, numerous types of ocular involvement have been described, such as uveitis, dacryoadenitis, episcleritis, chronic iridoscleritis, nummular keratitis, cataract, glaucoma, multifocal choroiditis, exudative retinal detachment, maculopathy, endophthalmitis, and optic neuritis^[2,6,10-14].

The largest series of ocular brucellosis was published by Rolando at al.^[3] in 2008 in their prospective study conducted in Peru through the years 1980-2005. Of 1551 confirmed cases of brucellosis, they detected ocular involvement in 52 patients (3.35%). Uveitis (82.7% of all cases), especially posterior uveitis (40.3% of all cases), was the most common form of presentation, followed by neuro-ophthalmologic complications



Algorithm 1. Flow diagram presenting number of studies screened, assessed for eligibility and included in the review

(13%), keratitis (5.8%), and conjunctivitis (3.8%). Most of the patients had chronic disease (86%) and females predominated (65%). Bilateral involvement was present in 20 cases (38.5%). The prognosis of the patients was generally unfavorable; 36 patients developed serious complications and 12 patients suffered complete vision loss. Prognosis was poorest in patients with panuveitis; eight of nine patients were legally blind after treatment, and five had no light perception. The authors noted that ocular damage occurs mainly in the chronic phase of the disease. Citing the work of Maini et al.^[15], who stated that cataracts, glaucoma, and maculopathies have been described as the most common complications of uveitis and are the main causes of different levels of visual loss, they concluded that early diagnosis of ocular manifestations of brucellosis was critically important^[16].

The other two largest series in literature were reported from Turkey, where brucellosis is still endemic. Güngör et al.^[5] presented 38 and Sungur et al.^[6] presented 28 cases of ocular brucellosis in which the prevalence was considerably higher compared to report of Rolando et al.^[3]. In addition, there were striking differences between the findings of the two reports. Güngör et al.^[5] reported a 26% incidence of ocular invasion, 71% of patients had chronic disease, 68.4% of cases presented with conjunctivitis, and 18% with uveitis. This study also reported the first two cases of dacryoadenitis and the second case of episcleritis in the literature as a part of ocular brucellosis. Sungur et al.^[6] reported a 21% prevalence of ocular involvement and 59% of patients with chronic disease. The most common presentation was uveitis (50%), mainly anterior uveitis (41%), followed by choroiditis (32%), papilledema (9%), and retinal hemorrhages (9%). Interestingly, distinct from the literature, all anterior uveitis cases were in the acute stage of the disease. In both studies, most patients had no major complications and no loss of vision was reported. As a common conclusion, both authors stated that ocular manifestations of brucellosis, either in the acute or chronic stage, were much higher than expected so all cases should have a detailed ophthalmologic examination.

Other studies in the literature were reported as sporadic cases^[17,27]. The case descriptions, treatment, and outcomes are summarized in Table 1.

Discussion

Despite eradication strategies such as conjunctival vaccination of livestock, Turkey is still accepted as an endemic country for brucellosis. The number of cases reported to the Ministry of Health decreased from 11,809 in 2011 to 5,148 in 2016. Ocular complications of the disease are thought to be relatively rare compared to other organ system involvement. Although ocular presentations associated with brucellosis have been known

PubMed					
Researcher/ year	Case (age/ gender)	Type of involvement	Treatment	Outcome	
Pagliarani ^[9]	24, F	Optic neuritis	Aureomycine + chloromycetin	Partial loss of vision	
	64, F	Bilateral uveitis + retinal	Aureomycine + PAS	Complete loss of vision	
	13, F	detachment	Aureomycine + PAS + streptomycin	Partial loss of vision	
		Bilateral uveitis + retinal detachment			
Foggit ^[19]	33, M	Anterior uveitis + retinal periphlebitis	Chloromycetin + streptomycin	Partial loss of vision	
Faran ^[10]	17, F	Endophthalmitis	Doxycycline + streptomycin + vitrectomy	Partial loss of vision	
Tabbaraa nd Al-Kassimi ^[18]	34, F	Uveitis	Doxycycline + rifampin + streptomycin	Partial loss of vision	
Abd Elrazak ^[21]	13, F	Optic neuritis	Tetracycline + streptomycin + systemic steroids	Recovery	
Akduman et al. ^[20]	16, F	Panuveitis	Doxycycline + rifampin + streptomycin + vitrectomy	Partial loss of vision	
Güngör et al. ^[5]	38 patients	26 conjunctivitis	Doxycycline + rifampin		
	21 F	7 uveitis		Not mentioned	
	14 M	2 dacryoadenitis			
	Ages: 42.1±17.3	3 episcleritis			
Karapinar et al. ^[22]	15, F	Optic (retrobulbar) neuritis	Rifampicin + doxycycline + streptomycin + systemic steroids	Recovery	
Rolando et	52 patients	43 uveitis	Doxycycline + rifampin ± streptomycin +	17 complete loss of	
al. ^[3]	34, F	3 keratitis	topical steroids	vision	
	18, M	2 conjunctivitis		19 partial loss of vision	
		7 neuro-ophthalmologic involvement		16 recovery	
Sungur et al. ^[6]	28 patients	18 anterior uveitis	Doxycycline + rifampin \pm topical steroids	14 partial loss of vision	
	15 F	4 panuveitis		14 recovery	
	13 M	14 choroiditis			
	Age: 8-60 (38±11)	4 papilledema			
		4 retinal hemorrhages			
Bazzazi et al. ^[17]	29, M	Conjunctivitis + episcleritis	Doxycycline + rifampin + TMP-SMX + systemic steroids	Recovery	
Oray et al. ^[12]	26, F	Endophthalmitis	Doxycycline + TMP-SMX + ceftriaxone + topical steroids	Partial loss of vision	
Turkish Medline	e				
Özden et al. ^[27]	56, F	Uveitis	Doxycycline + rifampin + topical steroids	Recovery	
Hatipoğlu et	56, F	Uveitis	Doxycycline + rifampin + streptomycin	Recovery	
al. ^[23]	30, M	Uveitis	Tetracycline + streptomycin	Recovery	
Parlak et al. ^[24]	34, M	Optic neuritis + vitritis	Doxycycline + rifampin + ceftriaxone + topical steroids	Recovery	
Kırıkkaya et al. ^[25]	19, F	Papilledema + abducens nerve palsy	Doxycycline + rifampin + oral steroids	Recovery	
Mete et al. ^[26]	49, F	Dacryoadenitis	Rifampicin + ciprofloxacin + systemic steroid	Recovery	

Table	1.	Literature	review:	case/	case	series	of	ocular	brucellosis
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F: Female, M: Male, PAS: Para-aminosalicylic acid, TMP-SMX: Trimethoprim-sulfamethoxazole

since the first decades of recognition of the disease, there is still no convincing data about their incidence, as most citations in the literature refer to case reports. Within the last 60 years of literature, only three case series of ocular brucellosis were reported and two of them were from Turkey. Ocular involvement was more common than expected in both series, present in approximately a quarter of patients. Excluding these large series, we found six cases of ocular brucellosis reported from Turkey. Considering the reported incidence of ocular brucellosis in such an endemic area, we believe that this number is low. This could be due to a high proportion of unreported cases, and/ or ocular evaluation not being a routine clinical practice for patients with brucellosis.

Two possible mechanisms are thought to play a role in pathophysiology of ocular damage. One is mediated by the presence of *B. melitensis* in the acute phase of the disease and the second is mediated by specific antibodies and immune complexes present in the chronic phase. Rolando et al.[28] performed aqueous paracentesis in two ocular brucellosis cases and were able to isolate the organism in only one patient after 24 days of incubation. However, they detected positive intraocular agglutinations in all patients, suggesting the presence of specific immunoglobulins in the eye. They claimed that the immunoglobulins could act individually or through immune complexes and the deposition of immune complexes could alter the vascular permeability of the uveal tissue, producing acute transitory or recurrent uveitis. In the literature, only Faran^[10] isolated Brucella from the vitreous humor in a patient with endophthalmitis. We did not perform ocular puncture in our patients, as it is not a routine diagnostic procedure. One of the main disadvantages of routine aqueous humor analysis is the small quantity of fluid obtained, which limits the number of tests that may be done on a single specimen.

Although it may occur at any stage, ocular damage seems to be more common and severe in the chronic phase of the disease. According to the report from Rolando et al.^[3], 0.003% of children with a diagnosis of systemic brucellosis had ocular involvement. This finding supports the hypothesis as children rarely develop the chronic form of the disease. Brucellosis is a systemic disease that has a wide spectrum of clinical manifestations and may be difficult to recognize, especially in the absence of classical symptoms. This is particularly problematic with the chronic form and some rare presentations, such as ocular brucellosis, must be considered when making a differential diagnosis.

Our patient first presented with a considerable decrease in visual acuity and a diagnosis of brucellosis was made after etiological investigation. The patient had permanent severe sequelae despite appropriate treatment. We believe that in an endemic area such as Turkey, routine ophthalmologic evaluation of all patients diagnosed with brucellosis as well as testing for brucellosis in all patients who present with classical patterns of ocular brucellosis such as uveitis will facilitate immediate initiation of appropriate treatment and help prevent progression to chronic disease and severe sequelae.

Ethics

Informed Consent: Consent form was filled out by the patient.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.U.Ç., G.K., Concept: M.U.Ç., Design: A.I.O., Data Collection or Processing: A.I.O., H.Ö.Ö., D.Y.Y., Analysis or Interpretation: A.I.O., Literature Search: A.I.O., D.Y.Y., U.S., Writing: A.I.O.

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