

Approach to Systemic Infections Presenting as Red Eye

Jessica Cao^{1*} and Raymond Stein²

¹Faculty of Medicine, University of Toronto, Canada

²Department of Ophthalmology and Vision Sciences, University of Toronto, Canada

***Corresponding Author:** Jessica Cao, Faculty of Medicine, University of Toronto, Canada.

Received: July 04, 2019; **Published:** September 05, 2019

Abstract

Objective: This article attempts to highlight worrisome ocular features that can help to identify high risk individuals of whom prompt diagnosis, management, and referral is warranted for systemic infections.

Sources of Information: PubMed and MEDLINE were searched for the terms “ocular manifestations” and “uveitis”, followed by refining searches with additional words.

Main Message: We review several systemic infections that commonly present with ocular symptoms in the primary care setting. We also discuss red flag signs that warrant emergency referral. The etiology and treatment for such conditions are often not eye-based, but rather systemic. As a result, early detection and diagnosis is key to preventing deterioration of sight or other severe nonocular complications.

Keywords: Red Eye; Systemic; Infections; Approach

Abbreviations

STIs: Sexually Transmitted Infections; TB: Tuberculosis; HIV: Human Immunodeficiency Virus

Introduction

The acute red eye is an extremely common presentation in primary care. Symptoms may include redness, photophobia, and pain. Although most causes for red eye are mild and local, some may have systemic, nonocular etiologies. In many cases, ocular symptoms may be the only overt signs of a serious systemic infection. As such, it is important to identify the individuals at high risk of a serious underlying systemic illness warranting further investigation. In these cases, the diagnostic and treatment approaches are not ocular, but systemic. Correct diagnosis and timely treatment of systemic infections is crucial to prevent deterioration, including permanent vision loss and severe nonocular complications.

Sources of information

Initial searches were conducted on PubMed using terms such as ocular manifestations, systemic infections, followed by refining searches with additional terms such as tuberculosis, Lyme disease, and treatment. Treatment guidelines were obtained from Public Health Canada.

Discussion

History

Recognition of risk factors, signs, and diagnostic criteria for systemic infections when taking a history is extremely important. As diagnostic equipment for a full eye exam is limited in the primary care setting, taking a detailed history is the most powerful tool. History

can often identify common causative agents of the red eye, such as injury, foreign body, contact lens use, or contact with individuals with conjunctivitis. Systemic infections should always be considered on the differential diagnosis, especially in the absence of overt common ocular causes. A detailed sexual history is important as many sexually transmitted infections (STIs) can manifest in the eye. Travel history, including to wooded areas and tropical regions, can place suspicion towards certain infections such as Lyme disease, mosquito-transmitted illnesses, or tuberculosis. Pre-existing medical conditions must also be reviewed, such as HIV status, latent TB infection, and immunosuppressive therapy.

Sexually transmitted diseases

The red eye may be caused by STIs, many of which may stay dormant over time or have atypical presentations that first appear in the eye.

Known as one of the great mimickers, syphilis can manifest in almost any organ, including the eye. Primary ocular syphilis is rare and occurs when bacteria first enters the body through the eye. Secondary ocular syphilis can affect any layer of the eye, most commonly causing posterior uveitis and panuveitis. Large, granulomatous keratic precipitates may be visible in the eye. Groups at increased risk include men who have sex with men (MSM), and HIV-infected individuals. Although rare in the general population, prevalence of ocular syphilis is up to 9% in HIV-coinfected patients [1]. Symptoms can occur anytime from 6 weeks after exposure to years after [2]. There is debate on whether patients with syphilis and ocular symptoms should also undergo cerebrospinal fluid testing for neurosyphilis [3]. Treatment involves benzathine penicillin G 24 million units IM for ocular involvement only [4]. STI testing, including for HIV, should be conducted on each patient with ocular syphilis.

Gonococcal conjunctivitis, caused by *Neisseria gonorrhoeae* infection, presents classically as hyperacute onset of severe purulent discharge from the eye within 12 hours of acquisition. Chemosis, edema of the eyelids and conjunctival papillae are common symptoms. Although often described in infants caused by transmission during birth, adult cases are also observed, often due to introducing contaminated fluids into the eye. Vision is unaffected when the infection is limited to the conjunctiva. Conjunctival scrapings should be taken for Gram stain and Giemsa stain tests. Gram positive diplococci is characteristic for *N. gonorrhoeae* [5,6]. Standard treatment for adults involve single dose ceftriaxone 1g I.M. [5]. Topical ciprofloxacin ointment q.i.d. or drops q2h can also be given. Patients allergic to penicillin should be given a single dose of azithromycin 1g P.O. [5]. Sexual partners should be evaluated for STI status. A serious, rare complication of gonococcal conjunctivitis is corneal involvement. In this case, gonococcus can penetrate the cornea within 24 hours, leading to opened globe [7,8]. If the cornea is also involved, ceftriaxone 1g I.V. q12-24h is given and the duration is determined by treatment response.

Sexual partners should also be contacted regarding possible exposure and testing.

Non-sexually transmitted diseases

Tuberculosis (TB) is a multisystem disease caused by *Mycobacterium tuberculosis* infection and had a worldwide incidence of 10.2 million in 2017 [9]. Risk factors include exposure to infected individuals, travel to regions with high rates of TB, particular Africa and South Asia [10]. Symptoms can manifest in any part of the eye and can be due to either primary infection of ocular structures or the immune hypersensitivity response [11]. Asymptomatic latent infection may be present for many years prior to presentation. Over half of ocular TB cases are not associated with pulmonary symptoms [12]. Any uveitis with unknown etiology, recurrent, or resistance to treatment should be screened for TB. Diagnosis of ocular TB is mainly completed by clinical symptoms with testing, including a chest x-ray and the interferon-gamma release assays (IGRAs) [13]. The standard pulmonary TB treatment regimen involves rifampin, isoniazid, ethambutol, pyrazinamide for 2 months, followed by rifampin and isoniazid only for another 4 months [14].

Another emerging illness is Lyme disease, the most common vector-borne disease in North America with increasing geographical expansion in the past several decades [15]. Lyme disease is caused by *Borrelia spirochete* infection and is transmitted by ticks. Lyme disease follows 4 stages: early localized, early disseminated, late disseminated, and chronic. Although removal of ticks within 24 - 36 hours is ideal for preventing infection, ticks can often go unnoticed. Early symptoms occur 3 - 30 days after exposure and include the characteristic erythema migrans rash in 80% of patients, as well as flu-like symptoms. 10% of infected individuals demonstrate follicular conjunctivitis

in this initial stage [16]. Patients presenting with conjunctivitis with other systemic symptoms, history of being in a wooded area should be inspected for the erythema migrans rash and considered for Lyme disease. Diagnosis is mainly based on clinical presentation and risk of tick exposure but can be supplemented with an enzyme immunoassay screening test and confirmatory immunoblot test [17]. Early antibiotic treatment is crucial to prevent late stage complications such as arthritis, polyneuropathy and encephalomyelitis [17]. Treatment with doxycycline 100 mg, P.O. q12h for 14 days, or an alternative should be initiated even without testing results [17]. Later stages of Lyme disease can cause inflammatory conditions such as keratitis, uveitis, and iridocyclitis [18,19].

Red flag symptoms

Acute retinal necrosis (ARN) is a rare, aggressive type of retinal cell death most commonly caused by Varicella zoster virus (VZV) or Herpes simplex virus (HSV) infection or reactivation. Most cases of ocular VZV or HSV infection result in herpetic keratitis and/or uveitis that resolves after standard antiviral treatment. However, sudden vision loss in one eye is a sign of ARN, and can also be accompanied with redness, pain, floaters, flashes. ARN can cause irreversible loss of vision [20]. Immunosuppressed individuals are especially at risk. This is an emergency. Patients should be referred to the emergency department for urgent ophthalmology assessment and immediate diagnostic testing. Treatment aims to inhibit viral replication and typically involves acyclovir (1500 mg/m²/day) I.V. for 5 - 10 days, then acyclovir 800 mg P.O. 5X per day for 4 - 6 weeks [21].

Endophthalmitis

Rarely, red eye has been reported to be a presenting sign of endogenous endophthalmitis [22]. Endogenous endophthalmitis is most commonly associated with endocarditis, urinary tract and kidney infection, gastrointestinal abscess, cellulitis, and meningococcal infection [22,23]. Acute red eye with systemic non-ocular symptoms should warrant an urgent referral to ophthalmology for a full assessment. Early diagnosis and aggressive treatment with intravitreal and sometimes systemic antibiotics can preserve vision and minimize other sequelae.

	Risk Factors	Tests	Treatment
Sexually transmitted			
Syphilis	HIV+ MSM Exposure to infected persons	TP-PA, FTA-ABS, and MHA-TP (preferred) RPR, VRDL, EIA (screening)	Benzathine penicillin G 24 million units IM
Adult gonococcal conjunctivitis	Exposure to infected fluids	Conjunctival scrape for Gram stain, Giemsa stain	ceftriaxone 1g IV if corneal involvement, ceftriaxone 1g IM q12-24h if conjunctiva only, or ciprofloxacin 500mg p.o. BID for 5 days OR azithromycin 1g PO
Travel-related			
Tuberculosis	Travel to sub-Saharan Africa and South Asia	Tuberculin skin test, interferon-gamma release assays Chest x-ray	Standard 6 month TB treatment as per Public Health
Lyme Disease	Exposure to wooded areas, ticks	EIA (screening) Immunoblot (confirmatory)	Doxycycline 100 mg, P.O. q12h for 14 days
ARN	VZV, HSV infection/ reactivation	Polymerase chain reaction (PCR), antibody analysis	REFER! Acyclovir IV (1500mg/m ² /day) for 5 - 10 days, then acyclovir PO 800 mg 5X per day for 4 - 6 weeks

Table 1: Overview of diagnostic approaches and treatments for systemic infections that manifest in the eye.

Conclusion

Many systemic infections, such as TB, syphilis, Lyme disease, and *N. gonorrhoeae*, can manifest in the eye, which can sometimes be the only overt symptom. As a result, screening patients with unexplained or treatment-resistant eye symptoms for risk factors of these systemic infections, running the appropriate diagnostic tests, and urgent ophthalmology referral is crucial to receiving a timely diagnosis and treatment.

Conflict of Interest

There are no financial interests or any conflict of interest for the authors.

Bibliography

1. Balba Gayle P, et al. "Ocular Syphilis in HIV-Positive Patients Receiving Highly Active Antiretroviral Therapy". *The American Journal of Medicine* 119.5 (2006): 448.e21-448.e25.
2. Dutta Majumder Parthopratin., et al. "Ocular Syphilis: An Update". *Ocular Immunology and Inflammation* 27.1 (2017): 117-125.
3. "Section 5-10: Syphilis". Canadian Guidelines on Sexually Transmitted Infections (2010).
4. "Canadian Guidelines on Sexually Transmitted Infections 2016 Updates Summary". Canadian Guidelines on Sexually Transmitted Infections (2016).
5. Gerstenblith Adam T and Michael P Rabinowitz. "The Wills Eye Manual: Office and Emergency Room Diagnosis and Treatment of Eye Disease". 6th edition. Philadelphia: Wolters Kluwer (2012).
6. Costumbrado John and Sassan Ghassemzadeh. "Conjunctivitis, Gonococcal". StatPearls Publishing (2018).
7. Day AC., et al. "Don't Forget Gonococcus!". *Eye* 20.12 (2006): 1400-1402.
8. McElnea Elizabeth., et al. "Challenges in the Management of Neisseria Gonorrhoeae Keratitis". *International Ophthalmology* 35.1 (2015): 135-140.
9. Hmwe H Kyu., et al. "The Global Burden of Tuberculosis: Results from the Global Burden of Disease Study 2015". *The Lancet Infectious Diseases* 18.3 (2018): 261-284.
10. "Tuberculosis (TB)". Public Health Agency of Canada.
11. Alvarez Gonzalo G., et al. "Ocular Tuberculosis: Diagnostic and Treatment Challenges". *International Journal of Infectious Diseases* 13.4 (2009): 432-435.
12. Bouza E., et al. "Ocular Tuberculosis. A Prospective Study in a General Hospital". *Medicine* 76.1 (1997): 53-61.
13. "Canadian Tuberculosis Standards 7th Edition: 2014". Public Health Agency of Canada (2014).
14. Figueira L., et al. "Ocular Tuberculosis: Position Paper on Diagnosis and Treatment Management". *Revista Portuguesa de Pneumologia (English Edition)* 23.1 (2017): 31-38.
15. Levi Taal., et al. "Deer, Predators, and the Emergence of Lyme Disease". *Proceedings of the National Academy of Sciences of the United States of America* 109.27 (2012): 10942-10947.
16. Raja Harish., et al. "Ocular Manifestations of Tick-Borne Diseases". *Survey of Ophthalmology* 61.6 (2016): 726-744.
17. "Lyme Disease". Public Health Agency of Canada (2017).

18. Mora Paolo and Arturo Carta. "Ocular Manifestations of Lyme Borreliosis in Europe". *International Journal of Medical Sciences* 6.3 (2009): 124-125.
19. Lesser RL. "Ocular Manifestations of Lyme Disease". *The American Journal of Medicine* 98.4A (1995): 60S-62S.
20. Yanai Ryoji., *et al.* "Poor Prognosis of Elderly Individuals 80 Years of Age with Acute Retinal Necrosis". *American Journal of Ophthalmology Case Reports* 7 (2017): 107-112.
21. Shantha Jessica G., *et al.* "Advances in the Management of Acute Retinal Necrosis". *International Ophthalmology Clinics* 55.3 (2015): 1-13.
22. Smith JM., *et al.* "Acute red eye and back pain as a presentation for systemic illness: case report". *BMC Ophthalmology* 6 (2006): 31.
23. Yeung WL., *et al.* "Red eyes as the initial presentation of systemic meningococcal infection". *Journal of Paediatrics and Child Health* 39.5 (2003): 390-391.

Volume 10 Issue 10 October 2019

©All rights reserved by Jessica Cao and Raymond Stein.