

Conjunctivitis, an Overview on Differentials, Etiologies and Management Approach: Literature Review

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Abstract

Background: Conjunctivitis is a common eye presentation in practice, that can be caused by multiple etiologies that include viruses, bacteria, and allergies. The presentation is composed of conjunctival injection along with itchiness and discharge, among other symptoms. The slight differences between each etiological factor can lead the way to set a satisfactory management plan. Clinical experience is required in dealing with conjunctivitis as it is usually presented in a primary health clinic, thus knowing the red flags is important. **Objectives:** We aimed to review the

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literature looking for etiology of conjunctivitis, risk factors, clinical presentation, diagnosis, management, and possible complications of this disease. **Methodology:** PubMed database was used for article selection, gathered papers had undergone a thorough review. **Conclusion:** Conjunctivitis cases must be dealt with with extreme delicacy; as the history and physical examination are the key for appropriate diagnosis rather than laboratory and radiological testing. A holistic approach to treating the patient is the essence of a fruitful management plan. Moreover, patient education along with pharmacological treatment is the optimal solution. The prognosis of conjunctivitis is usually good and adverse complications, almost, limited to neglected cases.

Keywords: Conjunctivitis, Red eye, Adenovirus, Differential, Diagnosis, Risk Factors, Management.

Introduction

Conjunctiva is the most outer layer of the eye which covers both the sclera and internal aspect of the eyelids. Conjunctivitis, or as it is commonly known as pink eye, can be caused by multiple etiologies including viral, bacterial, and fungal infections along with other causes such as allergy and chemical injuries (Al-Ghamdi et al., 2020; Mohamed et al., 2018; Embaby et al., 2018; Narayana et al., 2020). Viral infections have the highest overall prevalence among etiologies, with the majority caused by an adenovirus (67.1%) according to research was conducted in Saudi Arabia. (Tabbara et al., 2010) Additionally, another study showed almost similar results with 62% of cases are due to adenovirus in Pennsylvania, United States. (Sambursky et al., 2007) Conjunctivitis is considered as a common presentation in practice which accounts for 1% of overall primary care office visits in the United States. (Shields and Sloane, 1991) The purpose of this review is to gather data around the topic of conjunctivitis; especially about its etiology, diagnosis, and management.

Methodology

PubMed database was used for the selection process, and the following keys were used in the mesh ("Conjunctivitis"[Mesh] AND ("Diagnosis"[Mesh] OR "Management"[Mesh] OR "Risk factors"[Mesh] OR "Complications"[Mesh])). The inclusion criteria were met if the articles included one of the following: conjunctivitis or conjunctivitis risk factors, evaluation, risk factors,

complications, management, and diagnosis. Exclusion criteria were all irrelevant articles that did not meet the aforementioned criteria.

Review:

Etiology

The etiological background of conjunctivitis can be chiefly categorized as infectious and non-infectious. Infections that can affect conjunctiva include all variants of pathogens; bacteria, viruses, and even fungi. On the other hand, non-infectious causes can emerge due to chemical contact, allergy, and/or rarely immune-mediated reaction. Viral conjunctivitis is the commonest among the other infectious causes, and luckily it has the best prognosis. (Sethuraman and Kamat, 2009) Adenovirus represents the vast majority of all viral conjunctivitis cases, as well it is closest to 70% worldwide of overall infectious conjunctivitis (Ishii et al., 1987). Other viruses can cause conjunctivitis; a recent study confirmed the possibility of COVID-19 induced keratoconjunctivitis. (Guo et al., 2020) Last but not least, allergic conjunctivitis is connected with type 1 hypersensitivity reactions, the most common four subtypes: seasonal and perennial, vernal conjunctivitis, atopic conjunctivitis, and giant papillary conjunctivitis. (Varu et al., 2019; Ono and Abelson, 2005) Details about the most common causative organisms are illustrated in Box 1. (Varu et al., 2019; Epling, 2012)

<p>Box 1. Common causative organism of conjunctivitis</p>	
<p>Viral</p> <ul style="list-style-type: none"> ▪ Adenoviral conjunctivitis ▪ Herpes simplex virus ▪ Herpes zoster virus ▪ Molluscum contagiosum 	
<p>Bacterial</p> <ul style="list-style-type: none"> ▪ <i>Haemophilus influenzae</i> ▪ <i>Streptococcus pneumoniae</i> ▪ <i>Moraxella catarrhalis</i> 	

Clinical Presentation

All three etiologies share one cornerstone symptom which is an itchy-red eye. The differences come in the other adjacent signs and symptoms. For instance, viral and allergic conjunctivitis come with watery discharge, whereas purulent discharge usually accompanies a bacterial one. Unique symptoms can differentiate the underlying cause of the conjunctivitis attack, as a history of atopy can be easily correlated to allergic conjunctivitis, mucopurulent discharge to bacterial, while the history of recent upper respiratory tract infection with viral ones. (Ryder and Benson, 2020; Mahmood, and Narang, 2008) Different symptoms of each type are enumerated in Table 1. (Varu et al., 2019)

Table 1. The common presentation of different etiologies of conjunctivitis

Type of conjunctivitis	Clinical manifestations
Allergic	
Seasonal/perennial	Bilateral Eyelid edema Periorbital hyperpigmentation Conjunctival injection Chemosis Watery discharge and mild mucous discharge
Vernal	Bilateral Giant papillary hypertrophy of superior tarsal conjunctiva Bulbar conjunctival injection Conjunctival scarring Watery and stringy mucoid discharge Limbal Horner-Trantas dots
Atopic	Bilateral Eczematoid blepharitis Eyelid thickening Hypertrophy of superior and inferior tarsal conjunctiva Conjunctival injection and scarring Watery and stringy mucoid discharge Can be associated with keratoconus and/or subcapsular cataract
Giant papillary conjunctivitis	Laterality Associated with contact lens wear pattern. Papillary hypertrophy of superior tarsal conjunctiva Mucoid discharge Severe cases: lid swelling, ptosis
Viral	
Adenoviral	Abrupt onset Unilateral or bilateral Bulbar conjunctival injection Watery discharge The follicular reaction of inferior tarsal conjunctiva Chemosis Preauricular lymphadenopathy Petechial and subconjunctival hemorrhage
Herpes simplex virus	Usually unilateral Bulbar conjunctival injection Watery discharge The mild follicular reaction of the conjunctiva. Vesicular rash or ulceration of eyelids Pleomorphic or excavated dendritic epithelial keratitis of cornea or conjunctiva
Varicella (herpes) zoster virus	Usually unilateral Bulbar conjunctival injection Watery discharge The mild follicular reaction of conjunctiva Punctate keratitis in primary disease Punctate or dendritic keratitis in recurrent disease

	Vesicular dermatomal rash or ulceration of eyelids Pleomorphic or nonexcavated pseudo dendritic epithelial keratitis of cornea or conjunctiva
Bacterial	
Nongonococcal	Unilateral or bilateral Bulbar conjunctival injection Purulent or mucopurulent discharge
Gonococcal	Unilateral or bilateral Marked eyelid edema Marked bulbar conjunctival injection Marked purulent discharge Preauricular lymphadenopathy Corneal infiltrate or ulcer
Chlamydial (trachoma)	Unilateral or bilateral Bulbar conjunctival injection The follicular reaction of tarsal conjunctiva Mucoïd discharge Corneal pannus Punctate epithelial keratitis Corneal opacity Entropion Trichiasis Preauricular lymphadenopathy Bulbar conjunctival follicles

Diagnosis

The diagnosis process of conjunctivitis cases has three fundamental corners; history, physical examination, and lab tests. The latter usually not used unless there is an indication of possible severe complication or delayed healing. A detailed history should be obtained from the patient to guide the examination and possible laboratory investigations if needed. Suggestive history of similar symptoms in another family member or colleague in school or workplace can insinuate the transmission route of the infectious agent. Moreover, a history of maternal infection with *Neisseria gonorrhoea* while the infant is vaginally delivered will narrow the differential diagnosis window to the lowest possible. (Seewoodhary and Stevens, 1999; Mallika et al., 2008) Thorough details of the current bout should be analyzed as well, and ocular chronological history that includes onset, an eye affected (unilateral or bilateral), prodromal, and associated symptoms. Further inquiry about past similar episodes, if any, and their treatment and response, type and amount of discharge, itching, pain, periorbital involvement, photophobia, vision changes, and corneal opacity shall be done. (Ryder and Benson, 2020) The physical examination must include an assessment of visual acuity, an external examination, and slit-lamp, (see Table 1 for findings). Bacterial culture for determining the species is not usually required, it is almost only indicated in neonatal conjunctivitis. Smears for cytology can also be considered as an option for neonates cases. (Mallika et al., 2008; Prentice et al., 1977) Conjunctiva biopsy is the last resort for refractory cases; ruling out neoplasm is a must in those situations. (Akpek et al., 1999) Both allergen skin testing and tear immunoglobulin E provide helpful

results in determining the triggers of allergic attacks of conjunctivitis and preventing recurrence in the future. (Leonardi et al., 2013; Leonardi et al., 2015)

Management

The management of conjunctivitis must be tailored according to the patient's unique status. Allergic conjunctivitis initially starts with patient education which includes eye-rubbing discouragement, artificial tears, and cool compresses application. Moreover, avoiding the source of allergy if it is well identified and feasible to do so is important. (Takamura 2018; Baab et al., 2020) All of the four allergic conjunctivitis subtypes, except for giant papillary conjunctivitis, should start their management with topical lubricants, anti-histamines, and mast cell stabilizer drops. Giant papillary conjunctivitis necessitates the removal of the physical allergen, such as contact lenses, before proceeding with the aforementioned topical treatments. If the condition is refractory to topical options, a referral to a specialist might be required for further investigations and treatment. A topical or oral corticosteroid might be considered in such a dilemma. (Takamura 2018; Baab et al., 2020; Rathi and Murthy, 2017)

Viral conjunctivitis mostly is caused by adenovirus which is self-limiting. The patient should be vigilant for 10 to 14 days after the onset of symptoms as the viral shedding is highly contiguous. Thus, the physician shall grant a sick leave certificate for school or work to the patient. (Ford et al., 1987) Symptomatic relief is the goal of the treatment options that can be provided. This includes artificial tears, topical antihistamines or steroids, oral analgesics, and cold compresses which may be used to alleviate symptoms. (ShinYoshi 2016) Herpes simplex virus-induced conjunctivitis usually is self-limiting as well, but treatment with topical ganciclovir 0.15% gel or trifluridine 1% was proved beneficial in relevant papers. (Croxtall, 2011; Wilhelmus 2015) While herpes zoster virus conjunctivitis has no recommended treatment unless the patient is immunocompromised, in such a situation an oral antiviral drug, e.g. acyclovir, might be indicated. (Colin et al., 2000)

Despite that bacterial infection can be self-limited, treatment with a suitable antibiotic might be required to prevent further complications, as it is the most serious in terms of possible unpleasant complications. In milder cases, treatment may halt the contagious status of the patient, hence an earlier return to school or work can be achieved. As there is no clinical evidence of which broad-spectrum antibiotic should be used in treating bacterial conjunctivitis, the usage of the most convenient or least expensive option for a duration of 5 to 7 days is usually prescribed. (Sheikh et al., 2012; Ohnsman, 2007)

Severe conditions may warrant a bacterial culture to identify the exact organism to treat accordingly with appropriate antibiotics. Methicillin-resistant *Staphylococcus aureus* has been isolated in plenty of bacterial conjunctivitis patients, so sensitivity and resistance culture in such cases is highly appreciated. (Freidlin et al., 2007) Lastly, if the culture, for example, was positive for *Neisseria gonorrhoeae* or *Chlamydia trachomatis*, treatment with

a systemic antibiotic, macrolide, cephalosporin, and/or tetracycline is indicated according to the national, regional, or hospital guidelines. (Update to CDC's Sexually transmitted diseases treatment guidelines, 2010, 2012)

Complications

In general, it is safe to say that conjunctivitis, per se, is benign. Serious adverse outcomes are seldomly to occur. Possible complications of viral and bacterial conjunctivitis include punctate keratitis, chronic infection, conjunctival scarring, corneal ulceration, perforation, and even blindness. However, all these complications are usually a result of negligence and not seeking medical care (Azari and Barney, 2013; Altan-Yaycioglu and Poyraz, 2018)

Conclusion

To conclude, conjunctivitis is a common presentation in both primary health care settings and specialist clinics. The variable etiologies for this disease mandate a close-up look into the history and physical examination. Supportive management and patient education play a major role in the healing process, and patient safety measures should be taken seriously to prevent the spread of infection. Furthermore, teaching patients about possible complications and warning signs to seek urgent medical help is vital. Symptoms-based treatment is considered the first line, as the disease tends to be self-limited, in both allergic and viral conjunctivitis, whereas bacterial may require an antibiotic prescription. An appropriate follow-up plan along with patient's compliance would significantly decrease the chances of developing sequelae.

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