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Conjunctivitis in the practice of a primary care physician – friend or foe?

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ABSTRACT

Introduction and purpose: Conjunctivitis is one of the most common ocular conditions that primary care physicians encounter. As a very frequent and usually benign disease, most cases do not require a referral to a specialist and are managed by the general practitioners. Apart from being a stand-alone condition, conjunctivitis may also be a part of clinical presentations of some systemic diseases – both infectious and inflammatory. By being well-recognizable by GPs it can serve as an indicator, pointing them towards possible diagnoses and indicating the need for further testing. On the other hand, numerous ocular conditions share similar symptoms with conjunctivitis, some of which may be vision-threatening. It is therefore crucial not to misdiagnose them as simple or benign conjunctivitis, because overlooking and neglecting these diseases may have serious health consequences, including vision loss. The aim of this article is to review the condition, drawing attention to these two aspects of conjunctivitis as particularly important in the work of a primary care physician – as both a possible indicator for other, systemic conditions, and a diagnostic challenge due to a symptom overlap with many more severe ophthalmic diseases.
Materials and methods: A review of literature was carried out using online platforms Google Scholar and PubMed. Articles were searched by entering keywords: conjunctivitis, red eye, primary care, general practice.
Description of current knowledge: Conjunctivitis is a common condition often seen by general practitioners. It has three main types: viral, bacterial and allergic. It can manifest as a symptom of systemic diseases and shares symptoms with other eye conditions. Conjunctivitis is generally self-limiting and doesn't require treatment. However, evident bacterial cases may benefit from antiseptic or antibiotic therapy to prevent complications and reduce transmission.

Keywords: conjunctivitis, red eye, primary care, general practice

Introduction

Conjunctivitis is a common ocular condition stemming from the inflammation of the conjunctiva – the semitransparent mucous membrane covering the surface of the eye outer to the corneal limbus and the inner surface of the eyelids. The most common symptoms depend on the etiology and include: redness of the eye, photophobia, pain or itching and tearing or purulent discharge in the conjunctival sac. It is usually a non-sight threatening, self-limiting

condition not requiring pharmacotherapy or any physical intervention, but it also should not be overlooked, because it can present as a symptom of more serious diseases, both infectious and inflammatory, or pose a risk of vision impairment. Conjunctivitis is a fairly frequent complaint of patients presenting to general practitioners (GPs) as, even though it is an ocular condition, the majority of cases are diagnosed by professionals other than ophthalmologists. This, and the fact that conjunctivitis is one of the most common ocular conditions, suggests that GPs should be knowledgeable about this disease and its management, especially as most cases are self-limiting and do not require the attention of specialized eye care professionals. Another reason for which primary care physicians should be familiar with conjunctivitis is that many cases can be highly infectious, especially viral ones. That may prompt them to increase their awareness of the proper procedures aimed at reducing the risk of transmitting the infection. However, there are cases which could be sight-threatening, present with specific complications such as e.g. pseudomembranes, or be a part of a more serious condition. The GPs should also know when to refer such patients to other specialities.[1,2]

Etiopathogenesis

Conjunctivitis can be divided into 3 main types, depending on the causing factors:

- viral: the most common type, caused by a viral infection, usually does not require intervention,

- bacterial: the second most frequent among the infectious types, caused by bacteria, usually lasts for 1-2 weeks and exhibits considerable improvement when treated with topical antibiotic drops,

- allergic: the most frequent non-infectious type. Based on hypersensitivity mechanisms.

There are also less common causes for conjunctivitis, such as inflammation due to chronic dry eye disease or caused by the use of medications e.g. glaucoma eye drops. Besides, specific subtypes can be distinguished within the main types, that require a different approach, for example bacterial conjunctivitis caused by sexually transmitted diseases.[2–4]

Viral conjunctivitis

Viral conjunctivitis is the most common type. It results from a viral infection, with Adenovirus being the most common, and other pathogens including Enterovirus and Coxsackievirus[4]. Being highly contagious, it is important to prevent transmission by employing hygiene and appropriate approach to the examination and management. Conversely, if the transmission is not actively prevented, it often leads to community-based epidemics in places like schools or medical institutions. The characteristic symptoms of this type include watery discharge in the conjunctival sac, increased tearing and a burning sensation. The viruses causing it are also frequently responsible for upper respiratory tract infections so patients presenting with viral conjunctivitis often have a history of e.g. a recent common cold or coming in contact with an infected person. The infection being previously present can also be suggested by regional lymphadenopathy As the nature of this type is

infectious, it can begin as unilateral and spread to the other eye within the first few days of its course.[2,3]

Bacterial conjunctivitis

Bacterial conjunctivitis is the less common type of infectious conjunctivitis. The pathogens may vary between adults and children. The bacteria more commonly affecting children include mainly*Streptococcus pneumoniae* and *Haemophilus influenzae.* The ones responsible for the disease in adults are *Staphylococcus* species, such as *S. aureus* and *S. epidermidis* ,*Streptococcus* species and Gram-negative bacteria such as*Escherichia coli, Moraxella* species or *Pseudomonas* species[5,6]. Typical of this etiology are: an acute onset and mucopurulent or purulent discharge. Patients also often complain of difficulty opening their eyes in the morning, as their eyelids are held together by the discharge. This type of conjunctivitis is not expected to last as long as the viral form and should subside within 7 to 10 days. It may persist for longer but is unlikely to exceed 3 to 4 weeks.[2–4]

Allergic conjunctivitis

Allergic conjunctivitis is caused by a hypersensitivity reaction to an allergen. The mechanism behind it is the type 1 allergic reaction. It involves the production of inflammatory cytokines by Th2 cells in response to contact with the antigen and the stimulation of B cells by said cytokines, which in turn synthesise IgE immunoglobulin, that is responsible for the degranulation of mast cells[7]. They release inflammatory mediators, such as histamine, prostaglandins and leukotrienes which cause symptoms typical of allergic conjunctivitis: redness and oedema of the conjunctiva, accompanied by swelling and erythema of the eyelids, formation of papillae on the conjunctival surface and the signature symptom- itching[2–4,8].

Conjunctivitis as a symptom

Conjunctivitis, apart from often presenting as an isolated conjunctival inflammation due to a local infection or irritation, can also be a manifestation of various diseases involving many other systems within the organism. Because it is a very common ocular condition encountered by primary care physicians, it is well- known and can serve as a clue in the diagnosis of said diseases. Due to its recognizability, conjunctivitis often prompts further diagnostic investigation, guiding clinicians to consider and rule them out. The diseases that include conjunctivitis as part of their clinical presentation include both systemic infections and inflammatory diseases.

Systemic infections

Systemic infections that can present with conjunctivitis can be of both viral and bacterial etiology.

Among the viral diseases, one that has become particularly significant in the recent years is the SARS-CoV 2 infection, also known as COVID-19. A fairly important issue with this condition is a possible asymptomatic course. This means that, while transmitting the potentially severe disease, the patient can remain seemingly healthy. Conjunctivitis however,

may serve as the only presenting sign and symptom of this infection[9]. Taking this into account, a patient presenting with conjunctivitis and being possibly suspected of having COVID-19 should have their history thoroughly taken and be subjected to further diagnostic testing. Even so, it should not be treated as pathognomonic as approximately 10% of hospitalized COVID-19 patients present conjunctivitis[10]. Also worth noting is the fact that even in the absence of conjunctivitis, SARS-CoV-2 RNA may be detected in the ocular fluids during the infection[11]. This suggests that safety measures should be taken when examining the ocular region of patients suspected of viral infections. Regardless of the viral presence in the ocular tissues and fluids, conjunctivitis has also been proposed as a possible manifestation of the cytokine storm, resulting from the excessive immune reaction to the infection. This etiology may be similar to that of conjunctivitis in systemic diseases, such as Kawasaki syndrome[12].

Other viral infections that can have conjunctivitis as part of their manifestation include parainfluenza, which is, similarly to SARS-CoV-2, mainly a respiratory tract infection[13]. Measles should be among the possible diagnoses in the paediatric population, as conjunctivitis is considered a standard occurrence in this illness's course[14].

Systemic bacterial infections do not commonly present with conjunctivitis, but there are some examples in which this symptom is characteristic. One instance may be gonococcal conjunctivitis, caused by*Neisseria gonorrhoae.* In this case, the ocular symptoms are not considered to be caused by a systemic infection, but by auto-inoculation through contaminated hands or sanitary items, such as towels[15]. If their medical history suggests it, a patient with a bacterial conjunctivitis with severe mucopurulent discharge should be evaluated for gonococcal urethritis. The diagnostics should also include other sexually transmitted diseases, as they may be contracted simultaneously.

An example of ocular symptoms occurring as a systemic reaction to a bacterial infection is reactive arthritis. Its classic triad of symptoms includes arthritis, urethritis and conjunctivitis. The cause is presumed to be an erratic response of the immune system to a bacterial infection within the genitourinary or gastrointestinal system. This disorder, being closely related to a recent infection or risky sexual behaviour, underlines the importance of taking a thorough history and not overlooking conjunctivitis as solely a simple, stand-alone eye condition[16,17].

Inflammatory diseases

One of the diseases that include conjunctivitis as a principal clinical feature is Kawasaki disease. It is an acute vasculitis affecting children, usually younger than 5 years old. The inflammation involves the coronary arteries and, if untreated, the disease can lead to the development of aneurysms in these arteries. It is currently the most frequent cause of paediatric acquired heart disease in developed countries. Conjunctivitis is one of the prominent clinical features and it manifests in the initial stage of the disease's course. This may be helpful in guiding the clinician to consider Kawasaki disease early on, and a prompt diagnosis is crucial in preventing chronic damage to the coronary arteries and subsequent heart disease[12,18,19].

ANCA-associated vasculitis is a group of diseases caused by an autoimmune inflammation of the blood vessels. In their ocular manifestations, conjunctivitis is a common one. The form most associated with ophthalmic symptoms is granulomatosis with polyangiitis (GPA), in the other forms: eosinophilic granulomatosis with polyangiitis (EGPA) and microscopic polyangiitis (MPA) these manifestations are rarer, but may still occur. There is a tendency of the eye symptoms to occur early in the disease's course, giving conjunctivitis a potential to serve as an early indicator for further diagnostic testing if an inflammatory disease is suspected[20,21].

Conjunctivitis may also be present in systemic lupus erythematosus (SLE). It usually manifests as an element of keratoconjunctivitis sicca, caused by the involvement of lacrimal glands, leading to chronic eye surface dryness, irritation and also an upregulation of inflammatory cytokines[22]. The eye condition, if not accompanied by sufficiently noticeable symptoms from other systems, may simply resemble dry eye syndrome, so the presence of chronic conjunctivitis associated with eye dryness can serve as a suggestion to consider an inflammatory disease and conduct further testing.

Differential diagnosis

As conjunctivitis is one of the most common ophthalmic conditions general practitioners encounter, it is also important for them to be able to distinguish it from some other eye diseases. This is especially crucial for conditions that, unlike conjunctivitis, can be vision-threatening. The fact that some of these other diseases may put the patient at risk of their vision worsening underscores the need for GPs to be knowledgeable about the conditions that require management by a specialist and to know when to refer the patients for specialized care.

The main symptom that is common among both conjunctivitis and some other diseases that need to be ruled out is eye redness. The pathologies that may share this symptom are:

Acute angle closure glaucoma

This condition is caused by the increase in intraocular fluid pressure. The symptoms are: redness of the eye, ocular pain, blurry vision and rainbow- coloured halos around sources of light. The patients may also complain of headache, nausea and vomiting. If not treated, it can result in damage to the optic nerve fibres, leading to loss of peripheral, and later central vision.

Anterior uveitis

This condition, also known as iritis, stems from the inflammation of the anterior segment of the choroid- the vascular layer of the eye wall. The patients may display eye redness, ocular pain radiating to the brow and temple, photophobia and blurred vision. It may also lead to significant decrease of visual acuity, by causing complications such as cataract, or even vision loss.

Orbital cellulitis

Orbital cellulitis is a bacterial infection of the contents of the orbit. Its initial stage may share similarities with conjunctivitis, as both can happen after an upper respiratory tract infection – a sinus infection in case of the cellulitis. The eyes are also red, there may be eyelid swelling and pain. However, what sets it apart from conjunctivitis is the presence of fever and possible double vision. As it is a serious bacterial infection taking place very close to the central nervous system, it should be diagnosed and treated early to prevent damage to the nerves (e.g., to the optic nerve), or the further spread of the infection, such as to the meninges.

Eyelid conditions

As the conjunctivae are located on the inner surface of the eyelids and its remaining parts are covered by them, disorders concerning these structures can cause irritation and redness, bearing resemblance to conjunctivitis. They include blepharitis, which is the inflammation along the eyelid edges. It is often caused by the blockage of the palpebral glands and may result in redness, pain, burning or itchiness. The symptoms are often more noticeable in the morning which can show similarity to acute bacterial conjunctivitis. The treatment, however, is based on the hygiene of the eyelid edges and usually does not require the use of topical antibiotics.

Another eyelid dysfunction is trichiasis, which is the inward growth of the eyelashes. As they grow towards the ocular surface, the mechanically irritate and can damage the cornea and conjunctiva. This condition requires removal of the underlying cause, such as careful plucking out the eyelashes, usually with the help of a slit lamp or laser therapy.

Lagophthalmos is another condition that can lead to the irritation on the ocular surface. It means that the eyelids do not close completely. This leaves the conjunctiva and cornea chronically exposed to the surrounding air and, by evaporation of the tear film, leads to them drying out, causing irritation and even damage, such as corneal ulcers.

Similar to both previous conditions are entropion and ectropion. These mean the inward and outward turning of the eyelid, respectively. They can lead to irritation by either mechanical rubbing of the inward-turned eyelashes or the chronic air exposure and drying out when the eyelid is not properly covering the eye. Both of these can be corrected by eyelid surgery.

Subconjunctival haemorrhage

Subconjunctival haemorrhage is caused by a blood vessel under the conjunctiva bursting and the subsequent pooling of the blood in a space beneath the membrane. The result is eye redness. Its underlying causes may include hypertension, the use of anticoagulant medications or physical strain. In these cases the haemorrhage is typically benign, as it usually does not even cause any pain or discomfort. However, it is important to properly take a history, as a subconjunctival haemorrhage resulted from an eye injury may mask a more serious condition – the scleral rupture, which is the break in continuity of the eye wall.

Keratitis

Keratitis is the inflammation of the cornea, either infectious or non-infectious. It can exhibit findings similar to conjunctivitis, such as redness, ocular pain, foreign body sensation, discharge or eyelid oedema. Each condition is more common with contact lens wearers, making it necessary to properly take the patient's history and take both of them into account. What distinguishes keratitis from conjunctivitis is diminished vision and corneal ulcers, which can be visualized using a fluorescein stain under Woods lamp illumination during a slit lamp examination. If not treated, the corneal ulcers may cause opacification and significantly reduce visual acuity.

Foreign body

Conjunctivitis can both present with a foreign- body sensation and be caused by the irritation from an actual foreign body. This condition should especially be considered in cases with chronic inflammation that does not react well to treatment. The patient should be examined by a specialist considering the possibility of an occult foreign body.

Chemical burn

Patients suffering from chemical burns of the eye surface may exhibit findings similar to conjunctivitis- red eyes and a burning sensation. The condition should not, however, be overlooked, because it may involve the cornea and cause permanent damage to this structure, critical for visual acuity. For this reason, the patient should be referred to a specialist. It is also important to take a thorough history to find out the irritant, especially in cases like household chemicals, in order to tell its properties, such as whether it has an acidic or alkaline character and the time elapsed since the injury.

Dry eye

Dry eye syndrome, similarly to eyelid disorders, can cause chronic irritation in the mechanism of insufficient hydration and lubrication of the eye surface. The causes may range from imbalance in the tear film composition to autoimmune conditions, such as Sjogren syndrome. There is specialized therapy available, such as cyclosporine eye drops in cases that do not respond well to conservative treatment, but such patients should be assessed by an eye care specialist.

Nasolacrimal duct obstruction

This condition does not usually present with eye redness, as seen in the ones mentioned above, but the symptom it shares with conjunctivitis is increased tearing. Its cause is the blockage of the lacrimal pathways, which prevents tears from following their natural drainage path.

Instead, they pool on the eye surface causing the increased tearing. This tearing may lead to frequent eye rubbing and use of tissues, which can irritate the ocular surface. Obstructions in lacrimal pathways are often treated surgically so patients with this condition should be seen by a specialist.[2–4]

Diagnostics

A hygienic approach to the examination

Most cases of conjunctivitis presenting to GPs are of infectious etiology. Because of that, hygienic measures have to be taken to ensure that the possibility of transmission of the infection is minimised. These include the use of personal protective equipment, such as examination gloves and eye protection. A cotton bud should be used to touch the patients eyelids and the surrounding skin. As many cases are related to a viral upper respiratory tract infections, face masks should also be in use. Proper hand hygiene should be applied before and after the examination, and the used equipment should be disposed of in an appropriate manner in order to prevent spreading the infection to oneself, other patients or colleagues.

Infectious pathogens may be present on the patients hands, so after they leave the examination room, surfaces that may have been touched by them should be disinfected e.g. the doorknob, table surface, their seat or a pen.

In order to minimise the risk of spreading an infection, the patients presenting with symptoms suggestive of infectious conjunctivitis should be seen by the practitioner near the end of the work day, so that even if they were to bring highly infectious pathogens to the exam room, the number of people coming in after would be much smaller.[2,3]

Examination

The examination should include measuring the visual acuity, pupil symmetry and reaction to light, an ocular motility and double vision test as a basic neurological assessment. This should help exclude some of the vision-threatening conditions, such as pupils non- reactive to light suggesting an acute angle closure glaucoma or impaired ocular motility with double vision in orbital cellulitis.

Then, the eyelids and ocular surface should be examined. Instilling a topical anaesthetic, such as proxymetacaine, may be considered to aid the examination, however, the patients should be warned that it is only used to do that and it can not be treated as a pain relief method. The reason for that is the risk of tissue damage related to prolonged topical anaesthetic use[23]. In this part redness, oedema of the conjunctivae (chemosis) and the eyelids, the discharge and corneal appearance should be evaluated. When examining the eyelids, additional attention should be paid to the margins to look for signs of blepharitis, such as oily scales or greasy crusting of the eyelashes. Eyelid eversion should also be performed in order to visualize and examine the palpebral conjunctiva and the conjunctival fornix, as foreign bodies or papillae may be found there.

Apart from the ocular area, the lymph nodes of the head and neck should also be examined., especially the preauricular nodes. The presence of lymphadenopathy in these nodes may indicate a viral infection, or, less frequently, an infection caused by Chlamydia, Neisseria species, or local toxicity from medications applied to the ocular surface.[2,3]

Management

Prevention:

As with every other avoidable condition, preventing conjunctivitis is a major strategy against the disease. The approach to this prevention should concern the different causes. For infectious conjunctivitis, an importance of proper hygiene and stopping the transmission of pathogens should be underlined. This is essential in the population of contact lens users – the lenses should be kept and put on in a hygienic manner and replaced according to the specific recommendations. It is also advised not to wear them when swimming, either in pools or in natural bodies of water.[24,25]

Preventing the transmission of pathogens is also important in the case of an existing infection. This is particularly relevant for sexually transmitted diseases, as a gonococcal or chlamydial infection in the genitourinary tract can lead to transmission to the conjunctivae via auto-inoculation, meaning that a proper treatment applied early in the disease's course can prevent a potentially severe case of bacterial conjunctivitis[15].

In case of allergic etiology, allergen avoidance should be practised. Application of devices, such as air purifiers and regular cleaning is also advised.[8,25]

Preventing the condition can prove especially important in cases of epidemic cases. Due to the high degree of infectivity, a large number of people may contract the disease at the same time, placing a strain on the medical system due to the increased number of GP and A&E visits. This and the increased demand for medications can significantly raise healthcare costs[26].

Non-pharmacological treatment:

Considering the self-limiting nature of most conjunctivitis cases, the main line of treatment should involve managing the symptoms. A recommended way to address complaints like swelling, pain, itching and irritation is using cold compresses[25]. Additionally, some eye drops, even without active substances aimed at the pathogens, have been discovered to have a mild antiviral effect. The lubrication of the ocular surface provided by these drops may also alleviate some symptoms. For these reasons the use of artificial tears is recommended[25,27].

Pharmacological treatment:

As most patients with conjunctivitis do not require pharmacological treatment, it is important to recognise the cases that do call for it and may need to be referred to a specialist. The main issue here is the use of topical antibiotics. Even bacterial infections can resolve with just symptomatic management. In cases with significant symptoms, such as purulent discharge, the use of antiseptic or antibiotic substances may bring benefits. The suggested treatment is

starting with an antiseptic, as they do not increase the risk of developing drug resistance. In the event of the antiseptic being unsuccessful after 7 days, an antibiotic is recommended, preferably a IV generation fluoroquinolone[28–31].

The use of antibiotics may contribute to the development of drug resistance among the bacteria, especially multidrug resistant strains. Considering the high rates of resistance, antibiotics should be used when the bacterial infection is confirmed and other methods of treatment have failed[32–35].

There have been reports of the use of combined antibiotic and topical corticosteroid solutions for conjunctivitis[35]. This should be noted, as such combinations are contraindicated in the infectious form of the condition – by adding the steroids, an inhibitory effect is exerted on the immune reaction, allowing for the uncontrolled proliferation of viruses. This can potentially lead to vision- threatening complications, such as corneal opacification[3].

With paediatric cases, a bacterial etiology is the most common. Due to the specifics of this population, such as low compliance, potentially lower hygiene and frequent attendance at crowded places e.g. schools, the use of pharmacological treatment may be more strongly considered. Also, there are recommendations for when to refer children to a specialist: presence of symptoms such as vision loss, moderate to severe pain, constant blurred vision. When in doubt, GPs should also consider referring the children to an ophthalmologist[36,37].

Lastly, in allergic conjunctivitis topical anti-histamines or topical mast-cell stabilisers are recommended.[8,25]

Summary: Conjunctivitis is a common ocular condition seen by primary care physicians, resulting from inflammation of the conjunctiva, the semitransparent membrane on the eye's surface. Its main types are distinguished based on etiology into viral, bacterial and allergic. The patient's complaints include eye redness, pain or itching and tearing or purulent discharge in the conjunctival sac. It can occur independently or be a part of the clinical presentation in some systemic diseases, both infectious and inflammatory. This may be caused by the direct effect of pathogens on the conjunctiva or occur in response to the cytokine storm mechanism. By manifesting as a symptom of these conditions, conjunctivitis can serve as a clinical clue, prompting physicians to order further testing or consider specific diagnoses. This underlines the need to take a thorough medical history to avoid misinterpreting the patient's symptoms as only simple and benign conjunctivitis. The same is true for the other discussed aspect of the disease – the differential diagnosis. As many potentially severe ophthalmic conditions exhibit a similar presentation with eye pain and redness, it may lead to their misdiagnosis. A thorough history and examination, with attention to atypical features can help distinguish conjunctivitis from other, possibly vision-threatening diseases and an early diagnosis and treatment can prevent damage to the eye function, including vision loss. Since most cases of conjunctivitis are infectious, maintaining hygiene during the examination is essential. Due to its self-limiting nature, most cases can be managed with just symptomatic treatment. However, in

case of evident symptoms of bacterial infection, treatment with topical antiseptics is recommended, followed by antibiotic drops in case of treatment failure after 7 days.

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