

Common Ocular Manifestations of Sexually Transmitted Diseases

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Abstract

This review addresses the most significant ocular manifestations of Sexually Transmitted Diseases (STDs) which both ophthalmologists and sexual health physicians encounter during their practice. STDs to be discussed in this review include Syphilis, Gonorrhoea, AIDS and infection with *Chlamydiae*, Herpes simplex, human papilloma virus, Molluscum contagiosum, *Trichomonas vaginalis* and infestation with *Phthirus pubis*.

Keywords: Sexually transmitted infections; Ocular manifestations

Introduction

Sexually transmitted infections (STIs) are caused by some pathogens that can be acquired and transmitted through sexual activity. All of the major groups of microbes (i.e. viruses, bacteria, fungi and parasites) can be responsible for STIs [1].

In general, young people, especially in the age group 15-24 years, bear the greatest burden of STIs and account for about 50% of all new STIs. Both women and men are equally prone to contract STIs although the disease presentation and complications of untreated infections can be more pronounced in women, especially with some bacterial STIs, such as those caused by *chlamydiae* and *gonorrhoeae* [1].

The eye is a common site of affection, and nearly all sexually transmitted diseases (STDs) can have a significant ocular involvement. Ocular infection can occur as direct infection, as with gonorrhoea, or as indirect infection, as with acquired immune deficiency syndrome (AIDS). So, ocular examination and proper investigations should be a part of the routine assessment of the patients seen at STDs clinics to ensure prompt management of the ocular complications of STIs [2].

Gonorrhoea

Gonorrhoea is a common STD caused by a Gram-negative, intracellular diplococcal bacterium *Neisseria gonorrhoeae* [3]. Gonococcal diseases include: urethritis/cervicitis, epididymitis, salpingitis and pelvic inflammatory disease (PID) [4].

Highest incidence is in young, sexually active patients. A large number have symptoms of genito-urinary infection and mostly presented with burning sensation during micturition and penile discharge and about half of the women are symptomatic and may present with vaginal discharge and pelvic pain [2].

Ocular infection with gonorrhoea is often spread by autoinoculation or direct transmission from the genital secretions of an infected partner, and may occur both with and without associated anogenital infection. The conjunctiva is especially prone to invasion by *N. gonorrhoeae*. Once infection is established, the bacteria can rapidly invade the cornea, leading to keratitis. The keratitis initially will start at the peripheral cornea causing marginal ulcerations, coalesce to form a

peripheral ring ulcer, which may then perforate and can lead to endophthalmitis, if not promptly and adequately treated. These vision threatening complications can occur within 24 h of infection, requiring emergency identification and treatment of the infection [2].

The classical presentation includes a history of a painful red eye, marked lid edema and profuse mucopurulent discharge, severe conjunctival injection, corneal thinning, chemosis with white infiltrates involving the cornea. Visual acuity may be affected and depends on the degree of corneal involvement [5].

Gonococcal ophthalmia neonatorum is an ocular disease of newborn babies, caused by acquiring *N. gonorrhoeae* during vaginal delivery. If left untreated, it may lead to loss of vision. It usually presents within 2-5 days after birth. The practice of ocular prophylaxis is an important preventive method against gonococcal ophthalmia neonatorum [5].

Investigations

Any acute infection (urethritis, cervicitis, conjunctivitis) caused by *N. gonorrhoeae* is detected by the presence of Gram-negative intracellular diplococci (GNID) on a smear derived from urethral, vaginal or conjunctival specimens [3]. Culture isolation of *N. gonorrhoeae* used to be the gold standard test for *N. gonorrhoeae* infection. Cultures using selective medium, like chocolate agar, Martin-Lewis or modified Thayer-Martin are used for diagnostic confirmation [3].

Treatment

Gonococcal ophthalmia is a medical emergency, so red eye in a known Gonorrhoea patient should be viewed with a high degree of suspicion. For ocular infections, topical antibiotics like Gentamicin or Bacitracin applied frequently, achieve much higher ocular concentration than systemic treatments.

Treatment administered 6th hourly is usually sufficient for conjunctivitis. If there is corneal involvement, dual topical therapy hourly, day and night, is required [5,6]. Systemic treatment is with ceftriaxone 1 g intramuscularly (I.M.). If corneal involvement exists, or cannot be ruled out due to chemosis and eyelid swelling, hospitalization is required and the patient is treated with ceftriaxone 1 g intravenously (I.V.) b.i.d.

The duration of treatment depends on the clinical response, with a one day treatment sufficient for conjunctival involvement only. However, longer treatment is required if cornea is involved. In penicillin-allergic patients, Ciprofloxacin 500 mg orally single dose or Ofloxacin 400 mg orally single dose can be used [3]. Contact tracing to treat the sexual partners is vital. Gonococcal Ophthalmia Neonatorum prophylaxis involves application of 0.5% Erythromycin ophthalmic ointment preparation into both eyes of every neonate as soon as possible after delivery [3].

Chlamydia

Chlamydial conjunctivitis is an STD occurring most commonly in sexually active young individuals. Women are more susceptible than men. It is caused by *Chlamydia trachomatis* serotypes D-K(1,2). Epidemiologic data from WHO reported genital chlamydial infections as the commonest bacterium responsible for STDs the world over. Autoinoculation is considered the main route of transmission; however, inadequately chlorinated swimming pools, insects and other fomites could be other routes of transmission [6-8].

Both sexes can develop urethritis, proctitis, trachoma, and infertility. There can be prostatitis and epididymitis in men. In females, cervicitis, pelvic inflammatory disease, and acute or chronic pelvic pain are frequent complications [6,9,10].

Symptoms: Chlamydial conjunctivitis is often unilateral, but can involve both eyes. The patient usually presents with a subacute onset of red eye and mucopurulent discharge, which may become chronic, if ignored. Because of the similarity of these symptoms to those of viral and other bacterial conjunctivitis, many of these patients may have been previously misdiagnosed and managed with topical antibiotics without symptomatic relief [10,11].

Signs: Conjunctival injection, superficial punctate keratitis, superior corneal pannus, iritis and large follicles that are more prominent in the lower conjunctival fornices [7,11]. A follicular reaction is the hallmark of chlamydial conjunctivitis and usually affects the bulbar conjunctiva and semilunar folds. *C. trachomatis* is considered to be the commonest cause of chronic follicular conjunctivitis and accounts for 20% of acute conjunctivitis cases [11]. A palpable tender preauricular lymph node is almost always present [7,11].

Investigations:

Direct monoclonal fluorescent antibody microscopy of conjunctival swabs, which is fast and cheap. Enzyme-linked immunosorbent assay for chlamydial antigens and Polymerase chain reaction (PCR) [12].

Treatment:

Topical treatment is with tetracycline ointment four times a day for six weeks. Systemic treatment is with either Azithromycin 1 g single dose or Doxycycline 100 mg b.i.d. for 1-2 weeks. Contact tracing in order to treat sexual partners of patients is vital [4,13,14].

Syphilis

Syphilis is a multi-stage, chronic and progressively debilitating disease that is caused by a bacterial spirochaete called *Treponema pallidum*, which is often transmitted by a sexual route, can also be transmitted transplacentally in utero from an infected pregnant female to the foetus, and *via* blood transfusion. Based on the progression of

the disease, acquired syphilis is classified into early, late and Neurosyphilis [15].

The eye is not a common site of syphilitic infection. The pathogen usually spreads to the eye through the blood stream. Ocular syphilis can be caused either by the direct invasion of the spirochete or by an allergic reaction in tissues sensitized by the pathogen [15,16].

Almost any part of the eye may be involved in syphilis, including the sclera, cornea, lens, uveal tract, retina, retinal vasculature, optic nerve, pupillomotor pathways, and cranial nerves [15-17].

Ocular syphilis may mimic different ocular inflammatory disorders [18]. Therefore, a high index of clinical suspicion is crucial for the proper diagnosis [15,18].

Ocular involvement is rare in Primary syphilis, but may involve the eyes in the secondary stage and, more commonly, in late, latent, and tertiary stages [18].

Clinical presentation

The corneal inflammation caused by syphilis is called interstitial keratitis, and is an immune-mediated, non-ulcerative and non-suppurative corneal stromal inflammation. This may be localized or diffuse, affecting one or both eyes, and there may also be an associated iritis, with or without keratic precipitates [15,17]. It can present as white infiltrates around the cornea and runs a prolonged course, not responding to conventional treatment.

Syphilitic iridocyclitis occurs in about 4% of patients with secondary syphilis. About half of these cases are bilateral [16,19]. Although most commonly presenting in secondary syphilis, iridocyclitis can rarely occur in primary and tertiary syphilis. This condition should be suspected in STD patients with intraocular inflammation resistant to conventional treatment [16,19].

Syphilitic scleritis presents in the same way as any other scleritis, but it runs a prolonged course, and is often resistant to conventional treatment.

Argyll Robertson pupil, the classic pupillary change seen in syphilis, occurs most commonly late in the disease, although it can be seen in early neurosyphilis.

The optic nerve and the 3rd, 4th and 6th cranial nerves may be involved during early neurosyphilis. Optic neuropathy is commonly seen in patients with secondary syphilis.

Progressive visual loss as a consequence of optic atrophy may be seen as a manifestation of tertiary syphilis [15,17,20]. Syphilis also can present as a necrotizing retinitis, involving the mid-periphery and peripheral retina [15,17].

Investigations

The diagnosis of this disease relies a lot on clinical manifestations, however the following tests can be used for confirmation:

Dark-field microscopy: Dark-field microscopic examination is the definitive method for diagnosing early syphilis. The characteristic slender, corkscrew rod-shaped appearance of *T. pallidum* is clearly seen on a dark-field microscopic examination of exudates or specimens from lesions of a primary or secondary syphilis patient [21].

Serological tests: Serology tests remains the mainstay for the diagnosis of syphilis; the available serological tests for syphilis are of

two types: the quantitative non-treponemal tests (e.g. Venereal Disease Research Laboratory, VDRL; and Rapid Plasma Reagin, RPR), and treponemal-specific tests (e.g. fluorescent treponemal antibody absorption test (FTA-Abs); *T. pallidum* passive particle agglutination assay (TP-PA) and various enzyme immunoassays [21].

Treatment of ocular syphilis

Parenterally administered Penicillin G is the drug of choice for treatment of all stages of syphilis. Therapy regimens can be chosen from a few options, which are (A) intravenous aqueous Penicillin G 12–24 mega units (MU) daily for two weeks or (B) intramuscular Procaine Penicillin 2.4 MU daily for two weeks, taken in conjunction with Probenecid 2 g daily or (C) oral Amoxicillin 3 g b.i.d. for one month.

Patients allergic to Penicillin may be treated with either oral Erythromycin or Tetracycline at 500 mg four times a day for one month [3]. Topical, periocular, and systemic steroids have an important role in the management of the ocular complications of syphilis [22]. Contact tracing is of vital importance as well [23].

HIV

HIV/AIDS is a multisystem disease, affecting the eye in upto 70% cases. All parts of the visual system can potentially be affected in patients with HIV [24].

Ocular complications of HIV are mainly a consequence of secondary opportunistic infections, other than complications of antiretroviral medications [24].

Herpes zoster ophthalmicus (HZO) affects about 5-15% of HIV patients. Kaposi sarcoma is a highly vascularized tumor, caused by human herpes virus type 8, commonly affecting the skin and mucous membranes. It is seen in about 25% of patients who are HIV positive [21,25].

More than 50% of HIV-positive patients exhibit anterior segment complications, like dry eyes, keratitis, and iridocyclitis. Varicella zoster virus (VZV) and Herpes simplex virus (HSV) are the most common causes of infectious keratitis in HIV-positive patients [21,25]. Iridocyclitis in HIV-positive patients is usually mild and frequently associated with retinitis due to CMV or VZV [21,25].

Cytomegalovirus is the most common cause of intraocular infections in AIDS patients and *Cytomegalovirus* (CMV) retinitis is the most common infectious ocular complication that may affect 30-40% of severely immunocompromised individuals [21]. Ophthalmologic examination including indirect ophthalmoscopy with a dilated pupil should be performed to view the entire retinal periphery. Diagnosis of CMV retinitis is made clinically by noting the appearance of ill-defined white lesions of the retina which may be associated with hemorrhages. Patients may present with single or multiple lesions in one or both eyes [26].

HIV retinopathy is the most common retinal lesion seen in HIV, often presenting as cotton wool spots. It occurs in as many as 50-70% of patients [25].

Infectious choroiditis is detected in 1% of ocular disorders in HIV-positive patients, with *Pneumocystis carinii* being the most common identified organism [4,25,27].

Pneumocystis carinii pneumonia (PCP) is the commonest systemic opportunistic infection in AIDS patients [25,27]. *Pneumocystis* choroiditis is usually an indication of disseminated systemic pneumocystosis in severely immunocompromised patients. The choroidal infection is classically bilateral and multifocal. Clinically, the lesions are multiple, yellowish, well-demarcated, and characteristically seen at the posterior pole.

Management of ocular complications

Most ocular opportunistic pathogens cannot be eradicated fully; therefore, their management requires life-long suppressive therapy [21,28].

Treatment of CMV retinitis depends upon both the on the site of the active retinitis and the immune status of the patient. It includes an initial induction phase of 2–4 weeks to inactivate the retinal infection through high-dose anti-CMV medications followed by a low-dose of maintenance therapy to prevent progression of retinitis. Systemic therapy includes intravenous (Ganciclovir sodium, Foscarnet sodium and Cidofovir) and oral drugs (Ganciclovir and Valganciclovir) [28]. Local treatment modalities include Ganciclovir and Fomivirsen sodium implants [28].

Oral Valganciclovir is the most recent medication approved for treatment of CMV retinitis. With its proven efficacy, it has now become a convenient and effective substitute to intravenous Ganciclovir for both induction and maintenance therapy.

Herpes

Herpes simplex virus 1 and 2 (HSV-1 and HSV-2), also known as Human herpes viruses 1 and 2 (HHV-1 and -2), are members of the herpes virus family, *Herpesviridae*. HSV-1 is usually acquired orally during childhood, but can also be transmitted sexually. HSV-2 is primarily an STD.

It is now apparent that both HSV types 1 and 2 can infect either region (eye and genitals). Primary infection may consist of a relatively nonspecific conjunctivitis; however, subsequent episodes of reactivations can involve the cornea. Corneal epithelial disease is manifested by the characteristic dendritic ulcers [23,29]. Clinically, watering, redness, blurred vision, and ocular discomfort are the most common presenting signs and symptoms [23,30].

Stromal keratitis occurs in almost 25% of cases of ocular herpes. In this condition, deeper parts of the cornea are involved, possibly due to an abnormal immune response to the original infection. In these rare cases, corneal scarring and thinning develop, which may lead to globe rupture, resulting in blindness. Other ocular manifestations of herpes are iridocyclitis and secondary glaucoma, which may be due to trabecular blockade or trabeculitis [30,31].

Human Papillomavirus

Human papilloma virus (HPV) is a member of the papilloma family of viruses that are more commonly found in sexually active patients in their 20s and 30s. More than 30–40 types of HPV are typically spread through sexual contact and infect the anogenital region [32].

Human papilloma virus infection of the ocular surface is common. Corneal and/or conjunctival squamous neoplasias have been linked to HPV 16 or 18. In addition, conjunctival papilloma, due to HPV

infection, is a common benign epithelial tumor that typically grows in a pedunculated or sessile exophytic configuration [33,34].

Molluscum contagiosum

Molluscum contagiosum is a virus, affecting the skin and the mucous membranes. It is caused by a DNA *poxvirus* called Molluscum contagiosum virus (MCV). There are four types of MCV: MCV-1 to MCV-4. MCV-1 is the most prevalent and MCV-2 is seen usually in adults and is often sexually transmitted [35].

The skin of the eyelid can be infected with the virus. The lesions are often 1–5 mm in diameter, with a dimpled center. They are commonly painless, but may become itchy or irritated [35,36]. If they are on the eyelid margin, there may be an associated secondary keratitis and follicular conjunctivitis [36].

Phthiriasis pubis

It is a disease caused by *Phthirus pubis*, a parasitic insect (pubic louse) infesting human pubic hair. It affects about 2% of the population worldwide. This species may also live on other types of hair, such as the eyelashes and eyebrows, causing phthiriasis palpebrarum or pediculosis ciliarum [37]. Pubic lice are usually acquired by intimate contact between individuals including sexual transmission, shared towels, clothing, beds or closets. Adults are more frequently infested than children.

Presentation

Pubic lice manifestations in the eyelids are uncommon in the general population. Patients can present with itchy eyelids. A magnifying glass or a stereo-microscope can be used for the exact identification of nits, nymphs, and adult lice which, under magnification, reveal the lice and their nits attached to the roots of the eyelashes. It is then advisable for the clinician to look for pubic lice manifestation in other parts of the body, especially the genital areas, and that of the patients' partners, if possible. The diagnosis is a clinical one [3].

Treatment

The lice or their nits can be manually removed using forceps. Infections of the eyelashes may be managed with petroleum jelly applied twice daily for 10 days or 1% permethrin lotion, phenothrin and carbaryl [38], keeping the eyes closed during the 10 min application. Further treatment to other affected areas will be needed to fully eradicate this problem.

Trichomonas vaginalis

Urogenital trichomoniasis can be transmitted by sexual intercourse. Direct physical contact facilitates parasite adherence and penetration of the mucosal surfaces, which consequently elicits a host inflammatory response. Similarly, direct and physical contact pathway is most likely required for parasite transmission to extragenital sites e.g. pharynx [39], respiratory tract and eye [40]. Exposure of the healthy conjunctiva to vaginal secretions harboring *T. vaginalis* parasites leads to conjunctival infection presented by conjunctival inflammation and a yellowish, purulent discharge from both eyes. Indeed, the paucity of reports in literature may not reflect the true incidence of ocular infections due to *T. vaginalis* [40].

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