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Review Article

Explicating the presentations of Acanthamoeba keratitis with special concern in the COVID-19 pandemic ambient

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Abstract

This article presents an overview of information regarding Acanthamoeba keratitis per epidemiology, host-pathogen interactions, clinical manifestations, risk factors, environmental implications, diagnosis, treatment and management as well as COVID-19 characteristics which may be taken into cognizance for suspected infected patients, researchers and ophthalmologic practitioners. Acanthamoeba spp. is pathogenetically ubiquitous in nature. Acanthamoeba keratitis is considerably an ocular-threatening and debilitating keratitis that exhibits contumacious characteristics which hinder or impede treatment or management. At inception, Acanthamoeba generally depicts atypical clinical features which are frequently misdiagnosed as other microbial keratitis. Fundamentally, it constitutes a rare corneal infection of which the aetiologic agent is the protozoon Acanthamoeba spp. in contact lens wearers, presenting features of severe ophthalmic distress, blurred vision, blepharospasm, ocular excoriation, extraneous entity sensation and photophobia culminating in aberrant visual functionality. These are perspicuously due to retarded prompt and adequate treatment and management. Personal and environmental hygiene, especially on the hands, face and ocular areas as advised for the COVID-19 protocol could prevent contamination and dissemination of Acanthamoeba keratitis infection. The differentiating relatedness of Acanthamoeba keratitis, COVID-19 ophthalmologic infections and other ocular problems may not have been clearly elucidated.

More Information

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Introduction

Acanthamoeba presents as a ubiquitous, free-living and single-celled protozoon occurring in contaminated and polluted aquatic, terrestrial and atmospheric ambient. Acanthamoeba keratitis usually constitutes an adverse ocular threatening corneal infection and aberration presenting diagnostic and management constraints and challenges [1]. Prior to the avant garde usage of soft-contact lenses, it was well-nigh impossible to envisage Acanthamoeba contumacious scourge in the fauna and human population.

Acanthamoeba was detected certain decades ago, and the problem commenced and reached epidemic proportions soon thereafter as an emerging and reemerging infectious disease. The infection was realized more in men and in non-hygienic contact-lens wearers, especially in water contact [2]. It is pertinent to have expansive information and knowledge regarding the disease with focus on major risk factors, ecological analysis, preventive modalities including COVID-19 protocol [3,4]. Ophthalmic aberrations may present and persist in COVID-19 infections or may manifest following recovery. In order to harness or curb the dissemination of the infection, it is proper to analyze veritable and specific signs, history', appropriate tests and diagnosis, initiate treatment and management of comorbidities of ocular diseases, such as Acanthamoeba keratitis with COVID-19 and ocular threatening sequelae.

Natural history

Acanthamoeba is a rare, and commonly misdiagnosed etiologic agent of corneal infection particularly in contact lens wearers and all age groups [5]. The Acantamoeba genus belongs to the phylum Amoeboza, subphylum Lobosa and order Centramoebidae. Acanthamoeba spp. are classifiable by the 18s rDNA sequence analysis into T1-T12 genotypes, and the Acanthamoeba keratitis commonly exists secondary to T4 spp. genotype. The frequent etiologic agents of Acanthamoeba keratitis are the Acanthamoeba castellani spp. and the Acanthamoeba polyphaga spp. The extant forms

of the Acanthamoeba spp are the active trophozoite and the dormant cyst. The former depends on algae bacteria, bacteria and fungi for its nutritional needs, exhibits retarded locomotion and asexual reproduction. The cystic form depicts depressed metabolic functionality, and survives in excruciating environmental niches, such as food scarcity, adverse alterations in dessication, pH, temperature, as well as elevated doses of UV-light. There is no extant sex predilection [6].

Host-pathogen interactions of Acanthamoeba

Ocular infection initially involves pathogenic adhesion to the surface of the cornea by means of mannose- and laminin-binding proteins resulting in phagocytosis, release of enzymes and toxins, such as acanthoporin, ecto-ATPase, glycosidases, neuroaminidase, proteases, phospholipases and superoxide dismutase [7]. Corneal epithelial deterioration, excoriation and apoptosis provide the latitude for stromal invasion with its consequent degradation leading to pathogenic corneal intrusion [8]. Acanthamoeba proteases may trigger impairment of the corneal nerves resulting in severe and debilitating pain with characteristic radial keratoneuritis depicted on slit-lamp examination. Remarkably, Acanthamoeba intraocular infection is seldom observed because of the pronounced response in the anterior chamber by polymorphonuclear leucocytes. Inclusive factors which ostensibly contribute to Acanthamoeba pathogenic mechanisms include its expansive dissemination, non-distinct structure and functionality, persistence and tolerance to vast magnitude of environmental stress, and easily facilitated metamorphosis into the trophozoite and cyst forms [2,5]. The wearing of contact lens results in corneal epithelium microtrauma and glycoprotein upregulation. Adherent surfaces exist more in soft than in hard contact lens, thus providing the Acanthamoeba trophozoite the expansive latitude to the cornea of soft contact lens users [5,9].

In certain cases, parasitic keratitis is a peculiar infection wherein corneal perturbation derives from (i) direct parasite inoculation through exogenous ambient; (ii) dissemination by means of endogenous proximal structures; or (iii) due to immune-mediated aberration secondary to systemic parasitic infection(s). These are prevalently from infections caused by Microsporidia spp. [2,10] and Acanthamoeba spp [2], as well as other parasitic agents [11]. Also, Acanthamoeba keratitis impacts on non-wearers of contact lenses, emanating from corneal abrasion or trauma. There are extant spatiotemporal variations between developed and developing nations [12] as well as vulnerable populations in the incidence of Acanthamoeba keratitis.

Acanthamoeba virulence, treatment and management resistance regarding keratitis are ostensibly correlated with the generation of the organism of low relative molecular mass protease MIP133. These are in response to corneal epithelial cell binding via a mannose-binding protein and the latitude of the Acanthamoeba to metamofphose into the resistant cyst stage from the trophozoite [13]. Complications of Acanthamoeba keratitis may result in fulminating bilateral panophthalmitis [14].

SARS-COV-2 or COVID-19

Globally, the Severe Acute Respiratory Syndrome Coronavirus-2 or SARS-COV-2, a novel coronavirus, otherwise known as the coronavirus disease 2019 or COVID-19 has triggered health consequences of undecipherable dimensions. The infection constitutes a multisystem [15] perturbation that also deranges the ophthalmic system as ophthalmologists report diverse presentations of the ocular infection. It has necessitated for individuals susceptible or exposed to Acanthamoeba keratitis to seek for accurate and optimum ophtalmologic or ophthalmic health guidance from ocular practitioners and specialists due to the elevated risk of contracting COVID-19 via the wearing of contact lens [16]. However, there is no extant evidence for an elevated risk to contract COVID-19 due to use of contact lens in comparison to spectacle lens. Also, there is no suppprtive evidence that the application of standard presciption spectacles are protective against SARS-COV-2 or several other transmission agents [17]. It is, however, postulated that COVID-19 is being implicated as the causative agent in diverse severe and deranging ophthalmic pathologies, such as anterior uveitis, conjunctivitis, optic neuritis and retinitis [18]. These pose avenues for expansive polemics whether Acanthamoeba keratitis is of potential significance for environmental and public health transmission of COVID-19. For instance, ocular presentations in the clinicopathologic aspects of SARS-CoV-2 are rare and seldom feature as the clinical spectrum [19]. The COVID-19 RNA was isolated from eye tissues, however, the indictment of the eye as an infection route has not been clearly elucidated. The most presenting complaint and presentation is conjunctivitis that has the potential of developing at any stage of the disorder. Consequences of viral and immune-mediated tissue derangement, activation of the coagulation cascade and prothrombotic condition propagated by the virus, the inextricably-linked comorbidities and therapeutic modalities contribute to the ocular findings [3,15].

Clinical microbial diagnosis

Acanthamoeba keratitis constitutes an emerging and reemerging clinical microbial, environmental and public health problem invariably resulting from expansive application of soft and rigid contact lenses. The number of cases associated with the infection may be increasing, but there are extant retarded diagnosis or misdiagnosis in a vast majority of the detected or reported cases. The clinical trajectory, specific and precise parasitologic and ophtalmologic diagnosis, drug and surgical treatment of Acanthamoeba keratitis depict atypical mycobacterial keratitis and infectious crystalline keratopathy emerging as potent varieties of infectious keratitis [20,21].

These are clinical manifestations of corneal infections correlated with contact lens wearers and corneal surgical techniques as presented in radial keratoplasty and invasive penetrating keratoplasty. The clinical settings of these infections are significant for reliable and veritable diagnosis for researchers and clinicians with improvements in rapid diagnostic procedures and treatment. However, challenges and constraints pertain to Acanthamoeba. Thus, Acanthamoeba is an environmentally widespread, non-flagellated free-living amoebic parasite implicated in Acanthamoeba keratis, a rare infection with increasing prevalence and prospective potency to cause ocular perturbation. The flagrantly detected Acanthamoeba spp. is A. castellani, while other varieties such as A. culbertson, A. hatchetti, A. polyphagia, and A. rhysodes are periodically detected and isolated from ocular infections [20].

An expansive ocular examination is pertinent for suspected ocular infection. Early determination on slit-lamp examination involves epithelioplasty with punctate keratopathy, epithelial or subepithelial infiltrates, pseudo dendrites, and perineural infiltrates [5]. Perineural infiltrates are salient determinants for Acanthamoeba keratitis but may undergo regression at later stages of the disorder [22]. On slit-lamp examination, characteristic findings of late-stage Acanthamoeba keratitis are ''ring-like'' stromal infiltrates and radial keratoneuritis, but satellite lesions, ulceration, abscess production, anterior uveitis coupled with hypopyon, and epithelial excoriation are commonly observed [23]. The impact of Acanthamoeba spp. may cause granulomatous amoebic encephalitis, a protracted CNS disease, frequently presenting in immunocompromized patients [24]. The CNS disorders result in varied epidemiologic arrays, distinct clinical patterns and unique pathologic characteristics prompting expansive treatment and management trajectories. Clinical presentations of superficial amoebic keratitis showed linear, polymorphous corneal epithelial changes [25]. Scanning slit confocal microscopy demonstrated a 26u diameter structure identical to an Acanthamoeba cyst in the anterior stroma with numerous ovoid bodies, ostensibly metamorphosed keratocytes, inflammatory cells or trophozoites in Acanthamoeba keratitis [26]. A case of incipient Acanthamoeba keratitis in comorbid herpes simplex keratitis and antiherpetic therapy revealed dendritiform epithelial keratitis, subepithelial opacities, linear stromal infiltrate, corneal nerve/radial keratoneuritis as well as overt swelling and hyperemia of the limbal conjunctiva [27]. Other findings include ring infiltrates, ulceration and stromal lysis [28].

Increased incidence of Acanthamoeba keratitis is evidenced in epithelial defective corneas and parasite-overwhelmed contact lens; Low calcium concentrations promote A. polyphaga adhesion to extracellular matrix proteins; but there are extant polemics whether calcium functionality is intracellular or on the cell surface [29]. In order of magnitude, it is exhibited via assay that Acanthamoeba binds to fibronectin < laminin < collagen, while adhesion is compromised by mannose [30]. Acanthamoeba spp. are predatory and free-living selectively disparate bacteria consumers. Adhesion to the trophozoite membrane by the bacteria food source is concurrent with internalisation and digestion. The pertinence of the bacteria food source for Acanthamoeba spp. correlates with the predilection of the bacterial species adherence to the trophozoite surface and its rate of internalisation. Adhesion of trophozoite and cyst to soft contact lens is stronger in the former than in the latter [31] depicting the functionality of adhesion to the contact lens in contracting Acanthamoeba keratitis infection. Acanthamoeba keratitis development may be occluded in the presence of Langerhans cells in corneas of parasite-burdened contact lens [32]. Also, potassium hydroxide mount provides for rapid diagnosis and differential diagnosis of Acanthamoeba and fungal keratitis [33], Mitochondrial DNA (mtDNA fingerprinting) evaluation as a tool to identify potential reservoirs of Acanthamoeba infection illustrated that environmental isolate inclusion expounded that the most common clinical isolates have recoverable partners from the proximity with ostensible spatial dissemination [34]. Due to its rapidity, easy access or availability, decreased labour-intensity, and realization of its 18s rRNA region to detect Acanthamoeba in clinical samples, as well as its sensitivity and specificity, it is clear that polymerase chain reaction is a remarkable improvement for Acanthamoeba detection [35]. The protracted clinical course, diagnostic challenges, rampant treatment failures, and the increasing incidence of the disease may impede detection of Acanthamoeba parasites antecedent to a corneal button for histopathologic examination. Histopathologic study of Acanthamoeba keratitis is indicative of a four-stage pathogenic trajectory: (i) an incipient infection with concomitant surface epithelial breaching; (ii) excoriated kerotocytes by rampaging trophozoites; (iii) inflammatory response induced by neutrophil polymorphonuclear leucocytes; and (iv) stromal necrosis due to leucocytic action [36]. A sign of Acanthamoeba keratitis is the absence of corneal stromal neovascularization on biomicroscopic and histopathologic study [37]. It is of utmost importance for accurate laboratory diagnosis, collation of data and result interpretation to curb Acanthamoeba-phobia among patients and the medical personnel [38]. These efforts may grant the latitude to promote and undergird community capacity for the surveillance and harnessing of Acanthamoeba in the environment [2].

Treatment and management

Acanthamoeba keratitis is a rare but adverse complication of contact lens usage. Acanthamoeba treatment defies effective management, however, treatment has a commendable success rate at early diagnosis or inception of the disorder. Delicate diagnostic signs in conjunction with microbiologic investigation is a prelude to veritable specific antiamoebal therapy. New insights are being provided regarding the risk factors, incidence and pathogenesis of contact lens-related

infectious keratitis. Acanthamoeba keratitis with its uniqie characteristics is perceptibly related with poor prognosis or outcome, even with the provision of intensive treatment, particularly in the later clinical course of the disorder [2]. Acanthamoeba keratitis incidence is ostensibly retarded due to increased awareness and sensitization on the emphasis for full and proper contact lens sterilization ab initio [39]. Treatment within a short period of diagnosis may result in retarded or decreased morbidity and good visual outcome [28]. Acanthamoeba keratitis patients have been treated with topical fluconazole and miconazole, systemic fluconazole, and topical corticosteroids [27]. Also, intensive treatment regimen of topical neomycin, propamidine and polyhexamethylene biguanide gradually deployed to a maintenance-level within a 2-week to 1-month duration as to monitor toxic effect manifestations [40], as well as intensive topical propamidine and neosporin [41]. Hexamidine diisethionate (Desomedine, a diamidine derivative) 0.1% eye drops have been effective on isolated Acanthamoeba strains [42]. Acanthamoeba trophozoites are susceptible to varied medications, such as antibiotics, antifugals, antiprotozoals, and antiseptics, but are resistant to these agents in cystic form with resultant extended infection duration [5]. The two classes of antiamoebics which are usually the first-line therapeutic regimen for Acanthamoeba keratitis due to their established cysticidal impacts are diamidines and biguanidines which can be applied jointly or severally [22]. Polyhexamethyl biguanide improved the diagnosis and treatment of Acanthamoeba keratitis [43]. Acanthamoeba keratitis has ostensibly remained adamant to treatment due to lack of antiamoebic agents whch may completely annhilate the implicating parasite. Graft survival could be of optimum benefit in quiet eyes but may be inhibited due to recurrent infection in inflamed eyes. Graft survival is grossly ineffective for active or bacterial keratitis, thus canvassing for prompt and early treatment on detection. Despite intensive medical and surgical procedutres, Acanthamoeba scleritis may present poor prognosis [44]. The assessment of risk factors, contact lens type and wear schedule showed that microbial keratitis was less prevalent in disposable soft lens wearers than in conventional soft lens wearers [45].

Oral immunization with recombinant mannose-binding protein shields against Acanthamoeba keratitis, and the protection correlates with elevated concentration of anti-MBP IgA in lacrimating protected animals. Usual human lacrimal fluid prevents IgA antibodies against Acanthamoeba MBP that may protect by means of the inhibition of parasite adhesion to host ocular apparatus [46]. In vitro cytopathic effect assays depicted that low lacrimation levels (10[mu}uL of undiluted lacrimation per millilitre of media) perspicuously inhibited Acanthamoeba-induced cytopathic effect. Also, human lacrimation presents IgA-independent factors which shield against Acanthamoeba-induced cytopathic effect by inhibiting the functionality of cytotoxic proteinases.

Discussion

Acanthamoeba keratitis constitutes a chronic debilitating corneal infirmity impacting contact lens wearers. Risk factors for Acanthamoeba keratitis include lack of disinfection and inadequate hygiene of hands, contact lens, water and surroundings as well as bathing and swimming wearing contact lens [47]. Acanthamoeba is undisputedly a preventable disorder in which the incidence is reducable through the improvement of hygienic contact lens use and manual hygiene, avoidance of contaminated or polluted water and contact lens, stringent application of constant lens disinfectants, regular usage of disposable contact lenses. Evaluation, information and communication for contact lens wearers to avoid unnecessary public water usage; and to conduct surveillance of Acanthamoeba keratitis patients to promptly identify incidence and other demographic alterations for the elucidation of exposure risk and regional variations as a fundamental ecological analysis [4]. There may decrement in the incidence of Acanthamoeba keratitis in developing countries in comparison to developed countries due to gross misdiagnosis, deficient diagnostic potential, dimunitive awareness of the characteristics of the ailment, underestimated incidence and prevalence [2,47]. Indubitably, findings from BLAST and phylogenetic analysis based on DNA sequences have established the pathogen as Acanthamoeba T4 [48]. Inasmuch as Acanthamoeba keratitis is sporadic in developing countries, the opportunistic pathogen functionality of free-living Acanthamoeba, as in cystoisosporiasis [49] must not be ignored, especially in cases presenting as non-specific symptoms of keratitis devoid of clinical response to empirical antimicrobial treatment and management.

Conclusion

The COVID-19 pandemic has prompted dire predictions and consequences about health and healthcare resources, and may offer less developed countries and vulnerable populations limited latitude to overcome any constrictive clinicopathologic ocular spectrum. In this COVID-19 pandemic era, the coronavirus is putting the pinch on healthcare resources, especially ocular problems in differentiating or diagnosing specific retinitis or microbial keratitis. There may not be any interesting alternative other than to promote encompassing detection, monitoring, evaluation, treatment and management of eye problems without resource depletion in healthcare personnel and fiscal budgetary measures.

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