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COVID-19 Manifestations in Anterior Segment of Eye

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ABSTRACT

The pandemic resulting from Coronavirus 2 (SARS-CoV-2) has affected a large proportion of the population throughout the world affecting people of all sorts. The contamination differs from asymptomatic, slight, or extremely life-threatening respiratory conditions. It can cause an impact on almost all organs involving various systems of the body. Ophthalmologists from around the world have reported instances of all sorts of contamination involving the eye. Conjunctivitis has proven to be the frequent manifestation to be present at a given stage throughout the infection. Direct damage as a result of the virus, immunologically mediated damage to the host tissue, activation of the coagulation pathway occurs through the tissue damage and the associated comorbidities including its medications are accountable for the pathogenesis of several manifestations mentioned subsequently. The viral genetic material is identified from the tissues obtained from the ocular site but the involvement of orbit or eye to be a factor for viral replication is still not certain. Ophthalmic manifestations could present as the characteristic presentation of infection or the incidence might increase several days after recovery. Ophthalmologists have to be vigilant keeping in mind the possibility of illnesses involving the eyes and orbit with SARS-CoV-2 so as to obtain applicable history, search for adequate signs, give suitable assessments and thereby put an end to the contamination as well as establish a proper treatment protocol to counter the dangerous ill desired complications of the infection.

It is absolutely important that the ophthalmologists take note and obtain an integrated knowledge on the aspect of ophthalmic conditions involved in the deadly infection in order to minimize the threat it possesses to the patients and the lifelong disability that may persist through its spread. The article mentions the necessary ophthalmic associations linked to the virus.

Key words: COVID-19, COVID-19 and eye manifestation, Anterior segment manifestation of COVID-19, Mucor mycosis.

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INTRODUCTION

Anterior segment manifestations of COVID-19

Conjunctiva and cornea

Follicular conjunctivitis: Conjunctivitis is the one of the leading cause of ophthalmic involvement which is being reported. In a huge amount of instances which are being recorded, Sindhuja, et al. stated that 11/127 (8.66%) of those who had complaints involving the conjunctiva. All those who are symptomatic stated of having redness in the eyes. The involvement of respiratory tract signs and symptoms has been related to congestion in the conjunctiva. A conclusive evidence of hand eye contamination was confirmed in multiple victims. However, this was denied to be of medical importance as a significant factor [1]. This did not co relate from the effects of a cross sectional study conducted with the aid of Chen et al. in 535 instances which confirmed that the hand-eye contamination turned into an independent factor which could be involved in the pathogenesis of conjunctivitis [2]. Chen et al. advised that ophthalmic involvement is mostly observed to occur in a week after the beginning of infection. The conjunctival swab turned out to be positive for 5 days, although with gradually growing values of replication of the virus [3]. Nayak, et al. mentioned the beginning of follicular conjunctivitis 28 days from the point of detected COVID-19 contamination in a middle aged male with various other systemic involvements of varying intensity. The conjunctival swab showed no amount of any kind involvement with bacteria or fungus growth. The conjunctivitis started to heal in few weeks by taking medications including lubricants and also moxifloxacin eye drops which were non-preservative. The authors additionally stated that the virus found within the conjunctiva might also additionally be present even after the nasopharyngeal swab turns to confirm to be negative for the covid virus [4].

Viral keratoconjunctivitis: Keratoconjunctivitis presents to be the early manifestation in an affected person with slight respiratory involvement signs has been mentioned by Cheema, et al. The affected person showed evidence of congestion, purulent discharge along with the complaint of photophobia and was taken into consideration as herpetic keratoconjunctivitis and furthermore linked to the deadly pandemic by several factors of confirmation. SARS-CoV-2 checking out carried out in only those who mentioned tour records of stay in Canada. The swabs from conjunctiva and nasopharynx each was confirmed positive. This case proves the significance of taking into account conjunctivitis as one of the leading symptoms of COVID-19 [5] In a case record reported by china, Guo et al. suggested a affected person with extreme COVID-19 contamination within the eye taken to be as conjunctivitis and presenting a few days after COVID-19 signs. In the primary presentation, the cornea was found clear, and the affected person had discharge which was viscous, the swab taken from the conjunctiva turned to be affirmative for SARS-CoV-2 genetic material with the aid of using Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) however was not found to be positive for Herpes Simplex Virus (HSV) and also adenovirus and this was done daily in the same manner. On the next day of the initiation of remedy with topical levofloxacin and sodium hyaluronate, the sample turns out to be negative. Patient recovered nicely inside one week however showed up with similar complaints as before and investigations showed corneal staining in the periphery of each eye within 5 days. This time the swab from the conjunctiva did not show any involvement of SARS-CoV-2 and Herpes simplex virus. However, the Interleukin-6 (IL-6) tiers indicated ten times rise within the affected eye. With an immune-mediated pathogenesis taken into consideration, topical application of fluoromethalone was commenced and affected person showed remarkable signs of resolution from the illness. Since the virus was obtained within the conjunctiva, the primary presentation of conjunctivitis had to be attributed to local inflammation and subsequent involvement through the means of virus. It turned into a localized involvement of the left eye with improvement seen inside 8 days. The relapse, with a prominent involvement seen in both eyes, on hand, was thought to be to be because of a cytokine surge because of an autoimmune reaction facilitated *via* the virus. The patient was advised regular follow up with judicious use of topical application of glucocorticoid which is recommended for a few weeks to minimize the occurrence of immune-mediated keratoconjunctivitis [6].

Hemorrhagic along with pseudomembranous conjunctivitis: Navel, et al. in France informed a case report of an old aged male affected person with extreme infection from the virus, admitted in Intensive Care Unit (ICU), showing gradually evolving signs and symptoms of hemorrhagic and pseudomembranous conjunctivitis within a matter of few days' time from the start of the systemic involvement. Treatment advised with oral azithromycin and dexamethasone drops for topical application and frequent debridement of pseudo membrane [7].

LITERATURE REVIEW

Conjunctivitis in young population: A 30 fold steep rise was observed with the prevalence of Kawasaki disease-like scenario in youngsters in a few areas of Italy with sturdy affiliation with COVID-19. This extraordinary presentation is called multisystem inflammatory syndrome in children (MIS-C). Kawasaki disease, in itself a type of vasculitis which is self-limiting, is related to various involvements within the eye including that of conjunctiva cornea or uvea [8]. In the information obtained on MIS-C, the ophthalmic tissue involvement is particularly limited to the involvement of conjunctivitis. MIS-C is typically mentioned to have a positive serology report for SARS-CoV-2 on swab from nasopharynx stating it to be a manifestation of a delayed immunological reaction to the viral infection. Treatment is initiated with the aim of reducing the systemic inflammation. Corticosteroids, immunomodulatory drugs and anticoagulants like aspirin all were used as the treatment in the related case reports available [9].

Episcleritis: An incidence which was of episcleritis was well documented as presenting feature of COVID-19 occurring in a young male as being mentioned by Otaif et al. Patient presented with chief complaints of foreign body sensation perceived in the eye and the detailed history, the patient mentioned nasal, episcleral along with congestion of conjunctiva along with blanching with phenylephrine. He, with time showed up with complaints indicating viral contamination 3 days since the ocular signs started [10]. Managna et al. stated a similar report of episcleritis which presented within a few days' time after the onset of signs and symptoms of COVID-19 contamination. Most instances which suggested episcleritis are found to be without any cause and self-limiting. Almost a 3rd of them have been linked with viral infections along with ebola, hepatitis C and recently with the arrival of another deadly virus, SARS-CoV-2 virus [11].

Eyelid manifestations: Eyelid involvement of the meibomian glands along the eyelids and lid margin telangiectasia or hyperemia was documented in 11/27 (38%) sufferers in the study carried out by Meduri et al. in Italy. Blepharitis turned out to be emerging new evidence related to COVID-19 [12]. It might also present itself as a delayed manifestation of the infection sp. the prevalence is likewise predicted to increase in the post-pandemic duration specifically in those survivors who have been associated with a pre-existing ocular surface alteration. Ocular manifestations of COVID-19 could be acute, (inside 7 days) or delayed (after 7 days). Even though diffuse follicular conjunctivitis can be located in either type, immune reaction is taken into consideration to play a primary function in the late occurrence of the complaints. It is a lot more diffuse, typically has a corneal involvement, and shows excellent improvement while being treated with steroids. The recurrent and relatively late patients turned out to have a comparatively severe

onset in comparison to early presentation of conjunctivitis [6]. Treatment was started with lubricants and the disorder turns to be self-limiting. Topical antibiotics can be used as an adjunct to avoid bacterial superinfection. Ribavirin was found to be effective in a fraction of cases [3] Topical steroids have some sort of association in immune-mediated keratoconjunctivitis and episcleritis. Delayed manifestations of the same have not been documented as of now.

DISCUSSION

COVID-19 first appeared in Wuhan in China in unfolded gradually with its effects all around the globe affecting all sorts of population in a defining manner eventually to be called put loud as a pandemic within a year. SARS-CoV-2 virus is an enveloped and single-stranded RNA virus from coronaviridae family. This illness developed because of the virus shows and manifests itself in a wide range of symptoms. It can begin with a milder form but can rapidly transform itself into a life threatening manifestation within a short duration of time. It is almost being concluded currently that it may have an outcome on nearly all organs belonging to the cardiovascular, neurological, and gastrointestinal systems. As a matter of fact, an ophthalmologist became the one to point out the virus in Wuhan and sadly he himself was affected by it which later turned out to be the cause of his untimely death. Ophthalmic manifestations are of a wide range not only in presentation but also in duration and the consequences. Wu et al. advised that ophthalmic conditions occurring because of the virus are flared up in those who are documented with systemic disorder with derranged blood and inflammatory tests [13]. The theories involving the means of transmission leading up to the eyes encompass direct inoculation droplets, spread of the respiratory contamination *via* the nasolacrimal duct including the lacrimal gland and also not to forget the haematogenous route [14]. Samples with Schirmer strips and swabs from the conjunctiva have confirmed the viral RNA in a small fraction of survivors. Low value of RT-PCR in terms of sensitivity, a significant difference in the viral load from samples obtained from conjunctiva as being compared to the nasopharynx, and the timing of samples not correlating with the stage disorder can be the reason for the low yield. A poor end result though would not swipe up the minor chance of the virus being found in tears or floor of the orbit and the virus in ocular samples does now no longer mean an active site of contamination. As mentioned above, there might be no proof of any sort of possibility of ocular tissues being involved by the virus Keeping the conclusions of various research are nonetheless blurred, it's far more useful to apply protective gears, slit lamp breath shields, and maintain proper screening strategies at the same time as analysing sufferers. The assessment of the related literature shows that there might be a minimum chance of transmission through the floor of the orbit. This may be due to the fact that the receptors involved in the ocular manifestations have a very low binding capacity as well as its well short in terms of quantity. The binding capability of the organism with the receptors which are present on the ocular surface is low because of a highly significant content which is lactoferrin found in the tears which prevent the virus from its attachment to heparin sulphate and proteoglycans thereby inhibiting the magnitude and intensity of the infestation. Serum IgA is also assumed to have a major role in terms of preserving immunity. The medicinal drugs which are sought to deal with COVID-19 additionally have ocular toxicities [15]. A prolonged and injudicious use of chloroquine and hydroxychloroquine can very well transform into a deadly retinal toxicity however it isn't predicted or visible with the quick duration of use for COVID infection. Lopinavir/Ritonavir can also additionally be the reason of the reactivation of autoimmune conditions. Ribavirin, though not used in the first line management of the disease, has been linked to the appearance of several other diseases which can get flared up like optic neuropathy. Tocilizumab has been found to increase the chances of retinal hemorrhages along with the characteristic cotton wool spots. Systemic corticosteroids are involved to be a leading factor in the development of diseases like cataract [16]. The danger of life-threatening fungal contamination in immunocompromised people cannot be emphasised enough. Central retinal vein occlusion was also found to be a feature in those receiving IVIG. These factors must be thought upon and applied in the daily practices while dealing with the highly deadly pandemic by the ophthalmologic society which can be a significant factor in controlling the disease spread [17].

The ophthalmic involvements can begin its onset at any given point in the course of the disease. Therefore a vigilant approach is needed so as to conquer the disease and its manifestations with all the means of treatment available at our side. A positive approach with the contribution from all the departments showing a multidisciplinary approach can be a huge factor to stop this disease [18,19].

CONCLUSION

The appearances of ophthalmic features amongst COVID-19 survivors have a varied range *i.e.* 2-32%. The relation with SARS-CoV-2 with any of the above mentioned conditions have not been established uphill this point. What exactly is the point of origin, what is the leading point of all the manifestations, how and what should be done to tackle the manifestations and its consequences form a big puzzle to solve in front of us. the exact approach needed to counter this disease and its life threatening consequences will only be established through extensive and relentless research not forgetting a multidisciplinary approach. This will require an enormous amount of sample data and a highly functioning research unit. The association of covid and eye manifestations have not been completely established. There is an ongoing investigation about the spread of the virus through secretions of the eye. There is an alarming situation setting up because of the injudicious use of corticosteroids and antifungals in sufferers with increasing frequency of a deadly manifestation in the

form of rhino-orbit-cerebral mucormycosis. Thromboembolic headaches are thought to be of significance. Studies set up for vascular occlusions in ophthalmic vessels in COVID-19 thereby aiding in the control of the disability causing manifestations are needed. Proper use of anticoagulants and its timely involvement in disease control also has to be looked upon. As the vaccination phase is being carried out worldwide, there is a chance of improvement in these manifestations thereby improving the overall occurrence as well as recurrence rates. There is a large fraction of countries expecting a rise or experiencing another range of manifestations due to development of several other mutated strains of the virus. For now, what the broad overview of the scenario tells us is the judicious use of all the treatment options at our disposal. Having a vigilant approach in early detection and identification of the disease will definitely help in the protection of the general population.

The most important step to be taken is the propagation of knowledge regarding the presenting complaints as well as the consequences one might have to face if the disease progression is neglected to a point where the available treatment options might turn out to be of no significance to the patient. The society should be well aware so as to identify and seek help at the right time to reduce the disability and mortality which is highly associated with the disease caused by the virus.

The ophthalmologic society throughout the world should be vigilant enough so as to share the findings and knowledge in a global manner to put an end to the sufferings caused. The multidisciplinary approach thus formed will be well equipped with knowledge and a treatment protocol which will aid in a timely intervention to prevent unwanted complications.

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