Varicella Zoster Virus Induced Acute Retinal Necrosis Following Acute Meningoencephalitis in a Patient with Presumed COVID-19

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Case Report

Keywords: Acute Retinal Necrosis, Varicella Zoster Virus. Coronavirus disease 2019, Meningoencephalitis, case report

Posted Date: August 6th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-54356/v1>

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Abstract

Background: To report the coincidence of acute retinal necrosis syndrome (ARN) following acute meningoencephalitis and presumed coronavirus disease 2019 (COVID-19) in an immunocompetent patient.

Case presentation: A 58-year old female presented to our emergency department complaining of sudden unilateral visual loss following a recent hospitalization for a viral meningoencephalitis. Magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) analysis, polymerase chain reaction (PCR) of the aqueous humor, reverse transcriptase polymerase chain reaction (RT-PCR) of the nasopharyngeal swab specimen, chest computed tomography (CT), and fundus photography were performed for the patient. Ophthalmic examination revealed severe ocular inflammation and yellowish patches of necrotizing retinitis in the right eye compatible with the diagnosis of ARN. The result of PCR on the aqueous humor was positive for VZV. The patient received one intravitreal ganciclovir injection and 10 days intravenous ganciclovir followed by oral acyclovir. The patient underwent COVID-19 screening tests; chest CT-scan showed the features highly suggestive for COVID-19 while the RT-PCR was negative two times. Two months later, BCVA reached 20/70 in the right eye. The anterior chamber reaction and KPs resolved and the vitreous haziness significantly decreased

Conclusion: A case of VZV induced ARN following acute meningoencephalitis was observed in association with presumed COVID-19. This could be an incidental finding in the pandemic era of COVID-19; however, it could also suggest that COVID-19 might trigger ARN in cases having latent herpes family viruses.

Background

Acute retinal necrosis syndrome (ARN) is characterized by yellowish patches of retinitis in the midperiphery, arterial retinal vasculopathy and ocular inflammation. The most recognized causes of ARN are varicella-zoster virus (VZV) followed by herpes simplex virus (HSV) type 1 and 2.¹

The association between ARN and neurological diseases, including meningitis and encephalitis, has already been demonstrated.² It is believed that both replicating and latent viruses can enter the eye through the optic nerve after brain involvement. Encephalitis secondary to VZV leading to ARN occurs very rarely and HSV 1 and 2 are the most common factors in post-encephalitis ARN.³

Several neurologic manifestations including headache, nausea and vomiting as well as anosmia have been concomitantly reported since the first reports of the new coronavirus disease 2019 (COVID-19) in Wuhan, China. A few cases of encephalitis have also been reported; however, the full spectrum of neurologic manifestations of COVID-19 is yet to be determined.^{4,5} Herein, we report the coincidence of ARN secondary to VZV meningoencephalitis in a patient with typical chest computerized tomography (CT) scan features of COVID-19.

Case Presentation

A 58-year-old woman was referred to the ophthalmology department due to severe drop of vision in her right eye. Before this presentation, she had been hospitalized in another hospital due to a sudden-onset neurological disorder manifesting as severe headache, vomiting and right hemiparesis. The patient noted a history of chickenpox in childhood. The lumbar puncture had revealed a profile suggestive of viral meningitis. The magnetic resonance imaging (MRI) showed bilateral asymmetrical signal hyperintensity of the cortical and subcortical white matter of the medial temporal lobes and left perisylvian region on fluid-attenuated inversion recovery (FLAIR) images. Although the result of PCR on the cerebrospinal fluid was negative for HSV types 1 and 2, the clinical findings were highly suggestive for a herpetic encephalitis. Therefore, treatment with intravenous acyclovir was started. While still in the hospital, she noticed blurred vision in her right eye and was referred for ophthalmologic examination.

At presentation, the corrected visual acuity was counting fingers at 4 meters in the right eye with a positive relative afferent pupillary defect. The slit-lamp biomicroscopy revealed moderate cellular reaction and flare in the anterior chamber with multiple medium-sized keratic precipitates. Signs of severe vitritis were apparent. Funduscopy revealed vitreous haziness and several yellowish patches of extensive and confluent areas of necrotizing retinitis with discrete borders at the periphery of the retina particularly in the inferior and nasal quadrants. Multiple foci of retinitis were also seen posterior to the equator (figure1) as well as patches of retinal arteritis. The margin of the optic nerve was blurred and elevated. The results of ocular examination were unremarkable in the fellow eye.

Despite the absence of any symptoms, a COVID-19 screening was performed for her before admission according to the regulations of the COVID-19 pandemic. It included chest CT-scan and reverse transcriptase-PCR (RT-PCR) of the nasopharyngeal specimens. The chest CT-scan revealed bilateral peripheral and rounded ground-glass opacities (GGO) that were highly suggestive of COVID-19 (figure2), while the RT-PCR was negative despite being repeated for two times. Human immunodeficiency virus (HIV) test was negative and CD4 to CD8 ratio was normal. Multiple arms of the immune system were investigated and all tests were normal. However, the result of PCR on the aqueous humor sample was positive for VZV.

With the diagnosis of ARN, the patient received two intravitreal injections of ganciclovir (2 mg/ 0.1 ml, Cymevene®; 500 mg; Roche, Basel, Switzerland) in addition to intravenous ganciclovir 350mg twice a day for 10 days that was continued by oral acyclovir 4gr daily. Oral prednisolone acetate 50mg daily and Aspirin 80 mg daily were also prescribed after 2 days and continued for 10 days.

Two months later, BCVA reached 20/70 in the right eye. The anterior chamber reaction and KPs resolved and the vitreous haziness significantly decreased. The borders of the retinitis sharpened and scar formation was started at the edges of the improving retinitis foci. No retinal detachment or involvement of the fellow eye was observed during a two-month follow-up period.

Discussion And Conclusions

ARN mostly remains a clinical diagnosis with vision threatening potential and is principally caused by herpes family viruses.¹ In our case, it was caused by VZV and occurred one month after a possible viral meningoencephalitis despite receiving systemic acyclovir. It is believed that antiviral treatment has an effect against the currently replicating viruses; however, persistent latent viruses in the central nervous system could still spread to the eye through the optic nerve with a lag of 1 month to several years.³

In our patient, we found chest CT-scan appearance very similar to the pneumonia caused by COVID-19 while the RT-PCR test was negative for this disease. It has been shown however, that the sensitivity of CT-scan is higher than RT-PCR for diagnosis of COVID-19; 98% compared to 71%, respectively.⁶ There was one possibility that the pneumonia was a manifestation of her VZV infection. Nonetheless, VZV pneumonia is a rare and serious complication of adult chickenpox and commonly causes numerous nodular opacities measuring 5–10 mm in diameter with halo sign, patchy GGO, and coalescence of nodules diffusely.⁷ Therefore, VZV pneumonia diagnosis was much less likely in our immunocompetent asymptomatic patient with bilateral multifocal peripheral GGO in the coronavirus pandemic context. Moreover, the peripheral features of the lesions were somehow specific for COVID-19 pneumonia.⁸

To address the patient's signs as a whole, the most probable etiology of encephalitis in our patient could be VZV based on the PCR result of the aqueous humor. Although VZV is the most common etiologic factor for ARN, the post-encephalitis ARN secondary to VZV occurs very rarely. This fact is partly explained by the low incidence of encephalitis as a neurological sequela of VZV. The neurological presentations of HSV typically involve encephalitis; however, VZV causes vasculopathy, hemorrhages and necrosis in the brain rather than inducing encephalitis.^{9,10}

Invasion to the central nervous system (CNS) is possible in almost all beta-coronaviruses including SARS-CoV and MERS-CoV. The entrance of the virus into the brain has been shown in experimental murine models infected with SARS-CoV and MERS-CoV. The autopsy of the patients with SARS revealed the genome sequences in the brain. The olfactory nerve was presumably the potential route of CNS involvement.¹⁰ Until the preparation of this manuscript, a few cases of COVID-19 associated encephalitis have been reported through the pandemic;^{4,5} however, the full spectrum of the disease has not been clarified yet.

In conclusion, we report a case of meningoencephalitis leading to ARN concomitant with chest CT-scan features of COVID-19. This could be an incidental coincidence of two infectious diseases in the pandemic era. However, this case could also suggest the possibility that COVID-19 might trigger ARN and encephalitis in cases with latent herpes family viruses. Nevertheless, this hypothesis needs to be approved by future investigations.

Declarations

Ethics approval and consent to participate

N/A

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and materials

N/A

Competing interests

The authors declare no conflict of interest.

Funding

The authors received no funding

Authors' contributions

KH, FK, AR, MN, NA, and AR all participated in the diagnosis, data gathering and drafting the manuscript. All the authors read and approved the manuscript.

Acknowledgements

We would like to acknowledge Atefeh Heidari who helped us in taking the photographs of the patient.

Abbreviation: ARN: Acute retinal necrosis; VZV: Varicella Zoster Virus; COVID-19: Coronavirus disease 2019; HSV: Herpes Simplex Virus; SARS-coV: Severe acute respiratory syndrome- Coronavirus; MERS-coV: Middle east respiratory syndrome-corona virus; FLAIR: fluid-attenuated inversion recovery. MRI: Magnetic resonance imaging; GGO: Ground glass opacity; BCVA: Best-corrected visual acuity

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Figures

Figure 1

Moderate vitreous haziness and several yellowish patches with discrete borders at the far periphery of the retina particularly in the inferior and nasal quadrants. Retinal arterial vasculitis is evident in the inferonasal branch.

Figure 2

Axial chest CT shows small bilateral, multifocal peripheral and rounded ground glass opacities.