SUBCLINICAL REACTIVATION OF VARICELLA ZOSTER VIRUS AFTER COVID-19 AS A POSIBLE CAUSE OF STROKE IN YOUNG PATIENT

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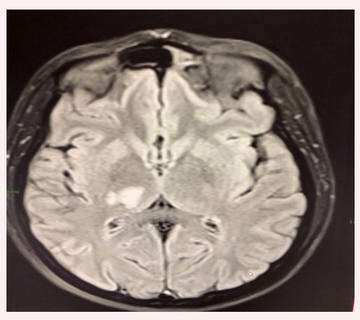
Introduction

Previous studies have observed an association between Varicella Zoster Virus (VZV) infection and stroke. Here we discuss possible causes of Herpes Zoster (HZ) due to COVID-19. Reactivation of VZV caused by decline of cellular immune response has been noted during the convalescent period or after recovery from COVID-19. Whether s troke can be a late sequel of a COVID-19 due to different inflammatory and coagulation mechanisms is currently uncertain. We present the case of a young patient with acute ischemic stroke, two months after mild COVID-19 infection associated with subclinical reactivation of VZV infection and discuss possible causes of stroke.

Case description

A 38 years old woman was admitted to the emergency department with acute onset weakness of the left arm and leg and walking difficulties. The patient did not have fever or changes in mental status. Physical examination revealed mild drooping of the left corner of the mouth and mild to moderate left hemiparesis. There were no other neurologic or physical abnormalities, nor nuchal rigidity. The patient had a recent past medical history of mild COVID-19 infection which was diagnosed through nasal swab by reverse transcriptase-polymerase chain reaction and she had been treated only with supportive therapy and recovered after one week from COVID-19 diagnosis. The patient has no comorbidities.

She underwent computed tomography of the brain that was negative. Magnetic resonance imaging of the brain showed ischemic area in subacute phase in right basal ganglia. CT angiography of cerebral and cervical vessels showed a discrete irregularity of the intimate contour of the ACI bilaterally without repercussion of the contrast display of the lumen.



Diffusion-weighted magnetic resonance imaging of brain showing acute infarct in right basal ganglia

Echocardiogram, electrocardiography and transcranial Doppler micro-bubbles test were normal. The results of laboratory blood tests, inflammatory markers, coagulation tests and d-dimer were also normal. Thrombophilia screening (proteins C and S, activated protein C resistance, antithrombin III, serum homocysteine, factor V Leyden, factor II, and MTHFR mutations) was normal. Markers of immune diseases (lupus anticoagulant, complement, rheumatoid factor, antineutrophil cytoplasmatic antibodies, antinuclear antibodies, antibeta2 glicoprotein antibodies, and antitransglutaminase antibodies) were negative. Serological testing for some infectious pathologies (Cytomegalovirus, Lyme disease, Toxoplasmosis, Herpes Simplex, Brucella, HIV, Epstein Barr virus, hepatitis viruses) were negative; only the IgG antibodies for COVID-19 and IgM (1,120) and IgG (4,62) antibodies for Varicella Zoster were positive. The patient underwent a lumbar puncture within the first week after stroke and cerebrospinal fluid (CSF) was normal and without detection of anti-VZV antibodies.

Discussion

An immunosuppressed state during covalescence or after recovery from COVID 19 infection that depresses certain cell subpopulation could be the possible mechanism of reactivation of VZV latency. It is thought that the occurrence of HZ infection correlates with a drop in the threshold of VZV-specific cell-mediated immunity (CMI) below an unknown level, while the severity of HZ correlates with the remaining level of this VZV-specific CMI at the time of reactivation.[1] Reactivated VZV, even subclinical can spread transaxonally from neural ganglia of cranial and peripheral nerves into the cerebral vessels. Previous studies to date suggest that in the patient who was confirmed VZV vasculopathy virologically, a productive viral infection with secondary inflammatory response can lead to pathological vascular remodeling with result of intima proliferation which contributes to vascular obstruction and ischemia of the the cerebral arteries, and with the damage of the media can result in thrombosis, occlusions, infarctions or aneurysms [2].

The occurrence of stroke in young adults without pre-existing cardiovascular risk factors after asymptomatic or mildly symptomatic COVID 19 infection is still unclear and under active research. As a possible mechanism is a proinflammatory process that triggers a hypercoagulable state.

Because of the positive VZ IgM serum antibodies result, indicating active infection without rash and a discrete irregularity of the intimate contour of the both ICA, it was hypothesized that the stroke could be secondary to VZV angiopathy. Low molecular weight heparin and intravenous acyclovir were started, with slow but steady improvement. The patient was discharged after 2 weeks with residual mild paresis of the left extremities and acetylsalicylic acid 100mg once a day.

Conclusion

In conclusion, it remains unclear whether subclinical reactivation of VZV infection may be the cause of stroke, whether other mechanisms in the convalescent period of COVID 19 infection, or a cascade of the same that can lead to stroke.

References

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