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COVID-19- postinfectious hypercoagulable state as a probable cause of basilar artery occlusion- Case Report

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Abstract

Covid-19 can manifest with serious neurological complications and hypercoagulability. Latest data from China showed neurological complications in 36% of 214 COVID-19 patients- mainly ischemic stroke. Coagulopathy associated with Covid-19 was reported to increase the risk of stroke also in young adults without comorbidities. A 29-year-old patient with hypertension admitted to the hospital with dysarthric speech and balance disorders and dizziness with vomiting was referred for thrombectomy of an occluded basilar artery after ineffective RTPA therapy. After the thrombectomy, a gradual reduction in the neurological deficit was observed-the permeability of the basilar artery was restored. However, during the intervention, the posterior right cerebral artery was damaged and a short-term extravasation of the contrast blood to the subarachnoid space occurred. MRI showed minor multifocal ischemic changes in the area of the cerebellum, pons and cerebral peduncle. In the pre-hospital interview a week earlier, transient changes in smell and taste were noted. On the day of admission, the patient had a negative antigen and PCR tests for SARS-CoV-2- virus. Laboratory tests showed high D-Dimers (5696 H ng /ml) and reduced fibrinogen. After mechanical thrombectomy, the patient reported double vision when looking straight and left. He was correctly oriented with slight ataxia and a deficit of strength in the left limbs, meningeal symptoms were negative. It is important to understand the association between Covid 19 and the possibility of an ischemic stroke and coagulation changes in order to choose appropriate stroke treatment methods.

Keywords: stroke, covid-19, hypercoagulable state, ischemic stroke, Coronavirus SARS-CoV-2

Introduction:

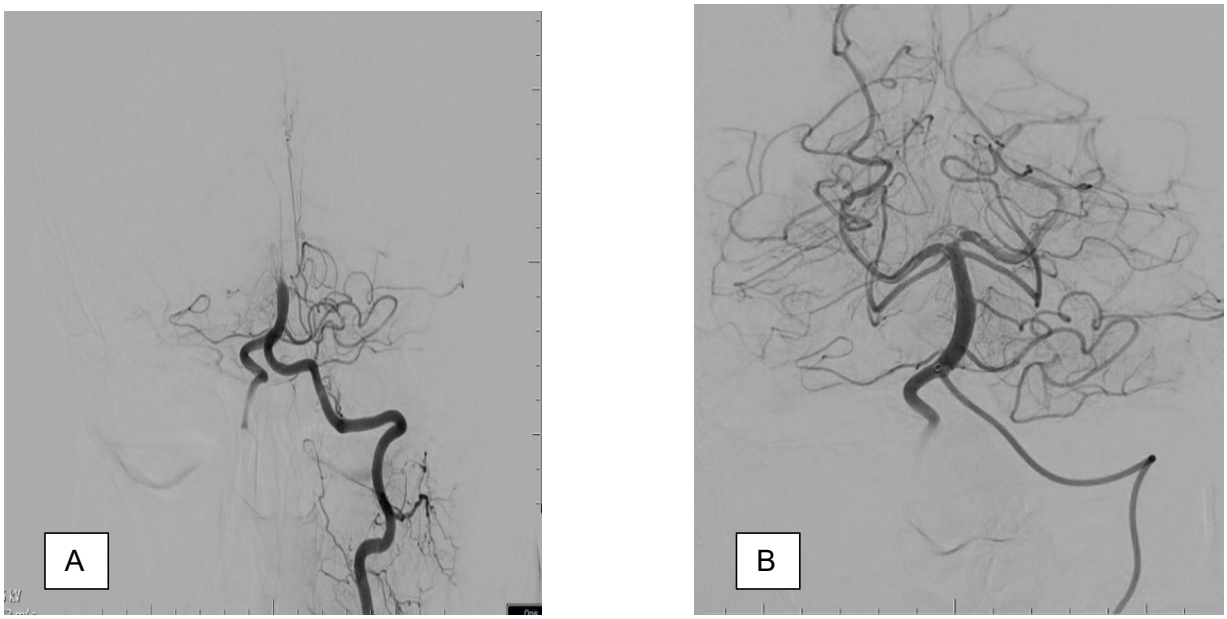
In late 2019 a new type of acute severe respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified by Chinese authorities and instantly spread across the world, causing the COVID-19 pandemic [1,2]. The epidemiological studies described dry cough, fever, headache and dyspnea with progression to pneumonia as the most common symptoms in the course of the disease [3]. However, there are some studies that reported COVID-19 as a multisystem inflammatory disorder that also affects the neurological system [4]. Early Chinese reports indicated that approximately 36% of patients hospitalized with COVID-19 presented neurologic symptoms, such as dizziness,ataxia, seizure, impaired consciousness, anosmia and stroke [5]. Moreover, among patients admitted to the hospital with COVID-19 infection, acute cerebrovascular disease has been reported in 2-6% [6]. It was investigated that cryptogenic stroke (stroke of undetermined etiology on TOAST criteria) in COVID-19 patients is characterized by a greater prevalence than in non-COVID-19 patients. Increased frequency of cryptogenic strokes may indicate hypercoagulability obtained during COVID-19 infection [7]. According to the literature, SARS-CoV-2 virus, capable of binding angiotensin-converting enzyme 2 receptors, may be the cause of cytokine storm and lead to a hypercoagulable state, which increase incidence of vascular thromboses [8,9]. For this reason coagulopathy in both, venous and arterial form of thromboembolism, is considered as one of the most severe complications of the disease with poor prognosis [10,11,12,13]. Additionally, hypercoagulable state associated with COVID-19 was reported as an independent risk factor that can be the cause of stroke and cerebral thrombosis, in young patients with no cerebrovascular risk factors [14]. A case series reported the presence of large-vessel strokes as an initial presentation among COVID-19 patients younger than 50 years old [15]. As the number of strokes noted in patients with COVID-19 in relation to the non-covid population is expanded according to the research [16], we would also like to enhance the increase in incidence of strokes in young patients and highlight the hypercoagulable state associated with covid-19 infection as an independent stroke factor.

Here, we want to present a case of a 29-year old patient with stroke of the trunk and right cerebellar hemisphere due to the occlusion of a basilar artery which was most likely caused by coagulopathy due to COVID-19 infection.

Case presentation:

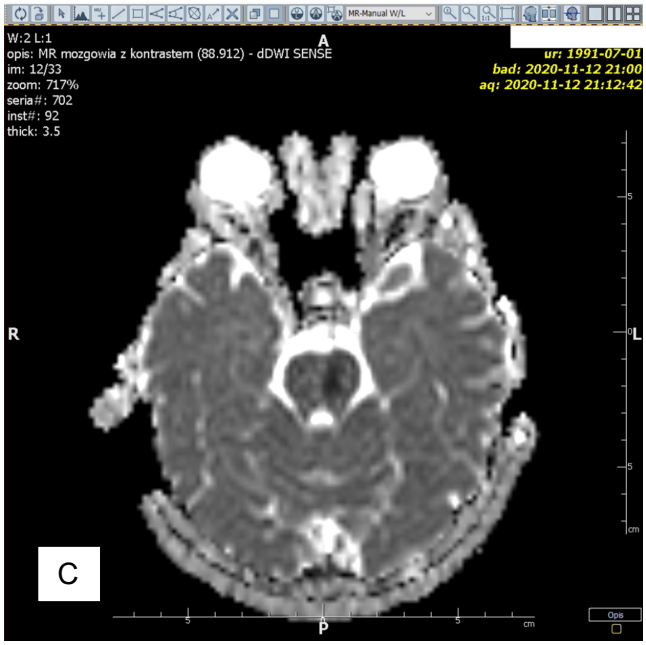
A 29-year-old patient with hypertension (without active pharmacotherapy) was admitted to the Neurology Department with dysarthric speech disorders, dizziness with vomiting, balance disorders and high blood pressure. After admission, tissue plasminogen activator (RTPA) was administered to the patient, but due to the lack of a beneficial effect, the patient was referred to the neurological department for thrombectomy of an occluded basilar artery. After admitting the patient, cerebral angiography within use of the Seldinger method was performed and showed obstruction of the basilar artery. The patient underwent urgent mechanical thrombectomy under general anesthesia due to life threatening condition. The treatment was performed using a hybrid technique (aspiration + Trevo). After the thrombectomy, a gradual reduction in the neurological deficit

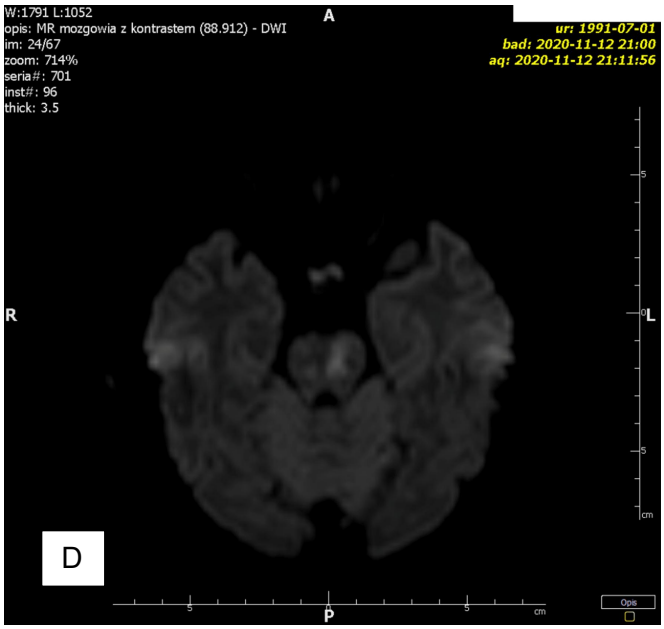
was observed - the permeability of the basilar artery was restored. However, during the intervention, the posterior right cerebral artery was damaged and a short-term extravasation of the contrast blood to the subarachnoid space occurred. Day after admission, the patient was referred for brain MRI with contrast due to a stroke of the trunk / right cerebellar hemisphere, in the condition after BA thrombectomy and with extravasation of blood at the pons on the right side. Minor multifocal ischemic changes were revealed in the area of the cerebellum, pons and limbs. Patient was referred for psychological consultation. His condition was defined as correctly oriented. He reported himself feeling unwell - dizzy and weak. In the pre - hospital interview a week earlier, transient changes in smell and taste were noted. On the day of admission to the hospital, the patient had a negative antigen test for SARS-CoV-2- virus, and a day after admission a PCR test for the RNA of this virus was performed with a negative result. In laboratory tests, attention was drawn to high D-Dimers (5696 H ng / ml) and reduced fibrinogen (0.93 L g / l), as well as reduced HDL value and increased triglycerides. During hospitalization, the patient's condition was stable. On the second day after mechanical thrombectomy, the patient reported double vision when looking straight ahead and looking left. The physical examination revealed that the patient was correctly oriented, meningeal symptoms were negative, with no obvious motor disorders, slight ataxia and a deficit of strength in the left limbs. The patient was not upright in the acute period of the stroke due to slight intracranial blood extravasation. The cerebral event was preceded by an episode of fever and anosmia that had resolved about 2 weeks earlier. Based on the aforementioned symptoms and positive Immunoglobulin-M Antibodies (IgM) and Immunoglobulin-G Antibodies (IgG), Covid-19 infection was retrospectively diagnosed. Despite extensive diagnostic work-up, including 48-hour cardiac rhythm monitoring, carotid ultrasound bubble test for right-left shunt, transthoracic and transesophageal echocardiography, head and neck angiography, hypercoagulability panel, no other apparent cause than post-Covid 19 hypercoagulable state was detected. Post- Covid 19 hypercoagulable state was thought to be a possible cause of AIS.



Cerebral Computer Tomography Angiography (Angio-TK).

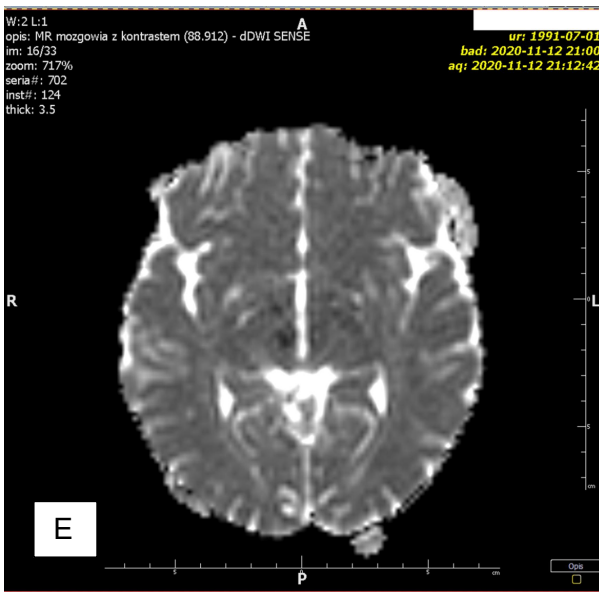
A. Obstruction of the basilar artery. B. Image of basilar artery angiography after mechanical thrombectomy.





Ischemic stroke of the pons. Magnetic resonance imaging (MRI) of the brain with contrast.

C. Diffusion-Weighted Imaging with Sensitivity Encoding (dDWI SENSE). D. Diffusion-Weighted Imaging.



Ischemic stroke of the right thalamus. Magnetic resonance imaging of the brain with contrast.

E. Diffusion-Weighted Imaging with Sensitivity Encoding (dDWI SENSE). F, Diffusion-Weighted Imaging.

Discussion:

Our study reports a case of ischemic stroke with minor multifocal ischemic changes revealed in the area of the cerebellum, pons and limbs in young patients with a history of COVID-19 infection. Covid-19 infection was diagnosed retrospectively based on the clinical symptoms described by patient and positive test for IgM antibodies and IgG antibodies, while diagnosis of ischemic stroke was confirmed by performed tests: magnetic resonance imaging (MRI) of the brain with contrast and brain computer tomography angiography (angio-TK).

According to the studies among patients diagnosed with COVID-19 the various neurological complications have been reported. The central nervous system manifestations included: headache, dizziness, seizures, encephalopathy, encephalitis, acute myelitis, intracerebral hemorrhage, microbleeds and stroke. The most frequent complications in the peripheral nervous system were Guillain-Barre Syndrome (GBS), followed by peripheral nerve palsy and anosmia [17]. Additionally, in many cohort studies, encephalopathy was reported to be the most common neurological manifestation in COVID-19 patients [18]. Based on studies conducted so far the presence of stroke has been described in 5.7% patients with severe COVID-19 and in 0.8% of patients with nonsevere disease's manifestation [5]. Early onset of cerebrovascular disease occurs more often in patients with cerebrovascular risk factors including: hyperlipidemia, diabetes mellitus (DM), hypertension, congestive heart failure (CHF), atrial fibrillation and deep vein thrombosis (DVT)[19]. According to the study conducted in New York the median age of COVID-19 patients, who experienced a stroke was 62.5 years [20]. However, an increased incidence of stroke in young patients with COVID-19, without associated risk factors has been reported [21]. The study showed a 7-fold increase in the incidence of large vessel stroke among young patients during COVID-19 pandemic than in previous years, which was probably related to SARS-CoV-2 infection [14]. A multicentre case series showed that from among 26 patients with COVID-19, who experienced haemorrhagic or ischaemic events , 27% were less than 50 years old [22].

As patients with acute ischemic stroke with COVID-19 experienced a significant increase in D-dimer levels, it can be assumed that COVID-19 infection initiates an inflammatory response and may cause hypercoagulable state and related ischemic stroke. According to the studies, in SARS-CoV-2 infection the mechanism of hypercoagulability is still not fully understood, however the connection between inflammation and thrombosis is suggested to have a crucial role [23]. Inflammatory cytokines release leads to the epithelial cells monocytes, and macrophages activation. Endothelial cells direct infection through the receptor of ACE2 and also cause activation and dysfunction of endothelial tissue factor expression, platelet activation and VWF and FVIII increased levels, all of which leads to thrombin generation and clot of fibrin formation [24]. For this reason, the state of hypercoagulability during covid infection requires great caution as it is characterized by high morbidity and mortality. Abnormalities in hemodynamic pathways are different than in other types of infections, ARDS and sepsis. The collected data suggest an unique, viral infection triggered, thrombo-inflammation mechanism, whose origin is in the pulmonary vasculature [24]. In the case of our patient, we observed an elevated level of D-Dimers (5696 H ng / ml). It should be enhanced that D-dimers have diagnostic significance in patients with

COVID-19 infection, as it was evidenced by numerous studies [25], [26], [27], [28]. Generally D-dimers are fibrin formation and degradation markers, which in COVID-19 infection reflect the hemostatic pathways activation. Elevated D-dimer and coagulopathy are known as indicators of higher morbidity and mortality [29].

To sum up, the collected data shows the importance of monitoring hemostasis parameters such as coagulation assays, platelet counts, D-dimer and fibrinogen when monitoring COVID-19 patients, as it has diagnostic significance and helps to manage the treatment [24]. Our work describes a clinical case suggesting the influence of COVID-19 infection on the occurrence of acute ischemic stroke in young patients who are not at high risk of stroke. It is important to recognize the neurological symptoms of COVID-19, especially ischemic, arterial or venous stroke. Hypercoagulability and rapid increase in cytokines are likely the causes of numerous systemic complications in COVID-19 patients. However, there is no solid evidence that this may be the sole cause of the large cerebral vessel occlusion [8,9]. Our case indirectly shows that this is a possible scenario. We believe that still more research should be conducted on this topic.

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