

Review Article

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A review on covid-19 and acute ischemic stroke, malignant cerebral edema & decompressive hemicraniectomy: A perfect storm; tackling this crisis by understanding it

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Introduction

In December 2019 the world was hit by new coronavirus pandemic with variety of symptoms. Neurologic manifestations have been reported as part of the different clinical presentation of the disease [1]. First reports came from China indicating a higher incidence of cerebrovascular complication associated with covid-19 [2]. With this published data Concerns about potential neurological complications of COVID-19 have been alarmingly increasing and obligated all researchers and clinicians to investigate this matter in a more serious fashion. Higher rates of strokes among patients with covid-19 has been discussed, but data regarding the outcomes of COVID-19 patients developing acute ischemic stroke due to large vessel occlusion (LVO) are limited [3].

Abstract

Since the world was hit by novel coronavirus pandemic, so many challenges for all healthcare providers have been arisen. It is safe to say that no specialty was singled out in the matter of different complication from this viscous covid-19 situation and neurologists and neurosurgeon were no different. There are some studied reporting neurological complication associated with coronavirus infections but when it comes to life threatening and acute neurological complications such as strokes and malignant cerebral edema the data is scant. Here we are going to review the possible pathophysiology of this phenomenon, the relationship between covid-19 and acute ischemic stroke and malignant cerebral edema by taking a closer look at current data regarding this matter.

Keywords: covid-19; acute ischemic stroke; malignant cerebral edema; covid-19 associated neurological complications.

Abbreviations: DHC: Decompressive Hemicraniectomy; ELVO: Emergent Large Vessel Occlusion; MCE: Malignant Cerebral Edema.

Acute Ischemic Stroke (AIS) is a life-threatening complication of coronavirus disease 2019 infection. New reports suggest an association between COVID-19 and AIS, although the underlying mechanism remains uncertain [4].

Cryptogenic stroke has been reported in 53 to 67% of AIS in COVID-19 patients [5,6].

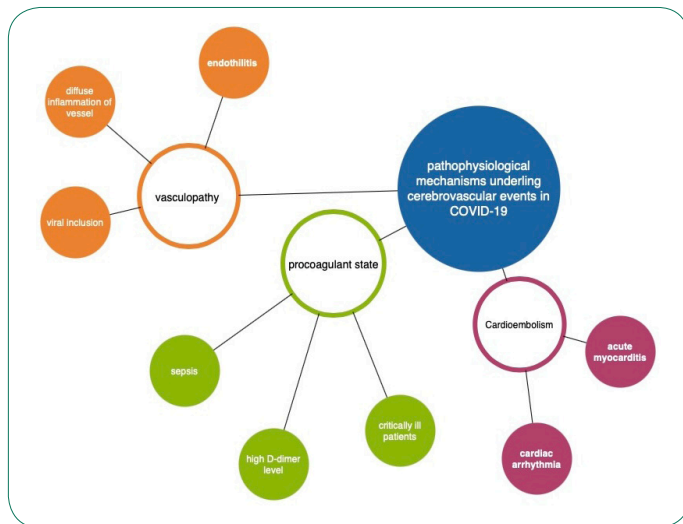
Malignant edema is a well-described consequence of acute ischemic stroke and can be worsened by the presence of hypercarbia induced by respiratory failure. Considering the higher incidence of cerebrovascular complications in patients with COVID-19, it is crucial for clinicians to be aware of the risk of rapidly progressive cerebral edema in the setting of respiratory failure of covid-19 infection and ischemic stroke [7].

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Here we are going to review the reports about covid-19 associated acute ischemic stroke and malignant cerebral edema by describing the pathophysiological mechanisms and detailed reported cases.

Pathophysiology

The main possible pathophysiological mechanisms contributed to cerebrovascular events are illustrated in this diagram.



As it is demonstrated above vasculopathy related to covid-19 infection and its cytokine causing endothelitis out of CNS vascular structures is one of the main mechanism [8,9].

Another mechanism attributed to this phenomenon is coagulopathy along with sepsis in critically ill patients with higher level of D-dimer [10-13].

A third possible mechanism is cardio-embolic stroke, as cardiac arrhythmia and acute myocarditis which are complication of cardiovascular system in covid-19 patients [14]. Cardioembolism was considered as the cause of AIS in respectively 15% and 24% of COVID-19 patients in two studies [5,6]. Finally, other rare causes of AIS have been reported in COVID-19 patients, including five cases of cervical artery dissections [1,6,15] and one case of focal cerebral arteriopathy in a 12-year-old boy [16].

Acute ischemic stroke (AIS) and Covid-19

Acute Ischemic Stroke prevalence has been reported about 1.3 to 4.7% of COVID-19 patients [17].

There have been some studies about ischemic stroke in covid-19 patients [18]. In a study in new York clinical presentation between two group of patients were assessed one with covid-19 and ischemic stroke the other without covid-19 and only ischemic stroke the results were informative and surprising, COVID-19 patients were younger, had higher admission National Institutes of Health Stroke Scale Score (NIHSS), higher peak D-dimer level, were more likely to have cryptogenic stroke subtype and a proximal large vessel occlusion, were more likely to be treated with anticoagulation, and had a higher inpatient mortality. The global COVID-19 Stroke registry including 174 patients from 16 countries confirmed that AIS patients with COVID-19 had a higher risk for severe disability and death [19].

Table 1: Acute ischemic stroke (AIS) & Covid-19.

Country	Study	Sample size	Onset of stroke during covid	Treatment	Stroke mechanism	Outcome	Covid respiratory symptoms
UK	Surveillance	153 57 with AIS	Not mentioned	Not mentioned	Large artery	Not mentioned	All with severe covid syndrome
UAE, Dubai	Case series	22	18 cases stroke was presenting symptoms 4 developed in first week	acute recanalization treatment in 2 Mechanical thrombectomy 2 Eight of 22 patients given therapeutic anticoagulation	predominantly large artery.	Six died, three from complications related to stroke and three from other COVID-19 complications. 14 with mRS disability score of 4	12 had lung involvement and respiratory problems
Spain	Cohort	841 11 with ischemic stroke	In 4 cases was presenting symptoms 10 days after onset of COVID-19 symptoms	therapeutic anticoagulation	The posterior arterial territory in 4 cases 2 cases of multiterritorial infarctions, 2 with arterial dissections	Not mentioned	11 had respirator involvement
China	Cohort	6 of 78 patients	2 presented with stroke	Not mentioned	Not mentioned	Not mentioned	5 of these patients had been categorized as severe COVID-19 and 1 had been categorized as non-severe

NYU Langone Health	retrospective case review	4 of 17 patients	All in first week of admission with no initial symptoms of stroke	therapeutic anticoagulation	large vessel ischemic stroke	Not mentioned	suspicious lung findings with multifocal, peripheral, ground-glass opacities in both lungs
Mount Sinai Health System, New York	Case series	5	From 2 hours to 28 hours after having covid-19 symptoms	therapeutic anticoagulation in all clot retrieval in 4 hemimcraniotomy in 1 stent in 1	large-vessel stroke	Discharged to rehabilitation facility 2 cases 1 discharged home 1 in ICU intubated 1 in stroke unit All after 2 weeks of diagnosis	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was diagnosed in all five patients.

In a surveillance study in UK on Neurological and neuropsychiatric complications of COVID-19 in 153 patients, 57 cases with acute ischemic stroke reported all with diagnosis of severe covid-19 and mostly the pattern of stroke was involvement of large vessels [5]. Because of the nature of this study it is important to pay close attention as many clinicians who is on the first line of admitting covid-19 patients considering the possible acute cerebrovascular events.

In a study in dubai 22 covid-19 patient with acute ischemic stroke were reported in 81.8% unfortunately stroke was the first symptom, with the use of surgical and medical treatment the mortality was significant (6 of 22). The pattern of stroke in this report was large territory infarctions. All patients were young adults [21]. This data shows the severity of covid-19 role ischemic stroke.

In a systematic review of 841 covid-19 patients with neurological manifestations, 11 cases were reported with ischemic stroke in 4 cases it was the first presenting sign. What is really interesting in this study is the fact that Unlike ICH, ischemic stroke occurred independently of COVID-19 severity, even in the absence of systemic manifestations. In fact, 4 patients had this serious complication in the recovery phase of the disease [1] which can be translated to the immense need of follow up of these patients also an emphasize on future guidelines in this particular matter.

In a large cohort study in Wuhan, China on neurological manifestation of covid it was reported 6 ischemic stroke cases

which 5 of them were categorized as sever covid cases. Like other studies 30% of cases presenting symptoms were ischemic stroke, there were no other data regarding the outcome of these cases [2].

Another surprising report is from a study in NYU Langone Health 17 covid-19 patients were under neuro imaging for completely unrelated reason to covid-19 but amazing findings were 4 of them showed symptoms of ischemic stroke. This particular report is alarmingly concerning because it expresses that sever respiratory symptoms of covid-19 is not necessarily an indicator or even a requirement for development of cerebral ischemic stroke [22]. This data is concerning and highlight the need of even more detailed and careful evaluation of patients

In another report from New York of 5 patients all diagnosed with severe covid-19 syndrome ischemic stroke with large vessel involvement was reported. The novelty of this report was the fact that all patients were younger than 50. And their mean NIHSS score (score used to determine severity of stroke) was 17, consistent with severe large-vessel stroke [23]. This is also an interesting topic for future studies to investigate the relationship between covid-19 and large vessel stroke in young population.

Malignant cerebral edema (MCE) and covid-19

The scarcity of available reports of covid-19 patients with acute ischemic stroke and malignant cerebral edema makes this issue formidable to discuss although because of the importance of this subject we have decided to review all possible data.

Table 2: Malignant cerebral edema (MCE) & Covid-19.

Country	Study	Sample size	Stroke pattern	Treatment	outcome
New York, US	retrospective single-center	7	ELVO in the internal carotid artery or middle cerebral artery	4 patients underwent decompressive hemicraniectomy (DHC) With only 1 death 3 mechanical thrombectomy and anticoagulant	4 of 7 died 2 in the first 24 hours of admission
Westchester Medical Center/ New York Medical College	Case report	1	Posterior division right MCA/parietal stroke no large vessel occlusion, indicating recanalization	Due to patient thrombocytopenia no anticoagulant therapy was administered	malignant cerebral edema/hemorrhagic transformation of the infarct in day 4 acute respiratory failure led to hypercarbia, likely potentiated the rapidity and severity of the cerebral edema. Patient has been Deceased
Philippine General Hospital	Case report	1	acute left internal carotid artery (ICA) infarct	Emergent left DH	Deceased due to respiratory failure
Italy	Case report – child	1	large right middle cerebral artery (RMCA) ischemia	bridging systemic thrombolysis followed by endovascular thrombectomy after MCE, urgent decompressive right-sided hemicraniectomy (DHC)	good functional recovery, residual hemiplegia.

In a study from a single center in New York all covid-19 patients with emergent large vessel occlusions with risk of developing MCE (risk was defined >50% of middle cerebral artery involvement on CT imaging) were reported. The risk assessment of 2 patient for MCE was not significant and they received medical treatment. 3 cases developed MCE and underwent DHC. The outcome of this group of 3 patients were good and only one mortality was reported due to the concurrent ST-segment-elevation myocardial infarction [24].

This report is showing promising results; COVID-19 patients with large territorial ischemic stroke can actually benefit from DHC and have a good outcome.

In a case report from New York one covid-19 patient with ischemic stroke surprisingly no large vessel involvement was reported after 4 days patient developed MCE and was deceased [7]. The key point of this report was the pathophysiological aspect of Hypercarbic respiratory failure associated with the development of fulminant cerebral edema [25]. Acute respiratory distress syndrome (ARDS) is a known complication of COVID-19 and can result in a severe and rapid respiratory failure leading to hypercarbia.

In another case report from Italy a 11 year old boy with serological evidence of covid-19 infection presented with acute ischemic stroke firstly managed medically but after 12 hours patient developed MCE and underwent emergency DHC which was successful [26].

The importance of this case report lies in the fact that pediatric patients are also in danger of developing the worst scenario caused by covid-19 crisis.

In one case report from Phillipine, a 36 year old female during home quarantine was presented with acute ischemic stroke and underwent emergency DH but due to respiratory failure patient was deceased [27].

Discussion

A meta-analysis showed that the incidence of acute ischemic stroke in COVID-19 patients ranges from 0.9 to 2.7% [4]. Acute ischemic stroke has been in some cases the presenting symptom of disease and it was not always with a linear pattern in association with covid-19 severity [20].

Because of the pattern of AIS associated with covid-19 is mostly large vessel [5]. Special attention is needed to be paid. Malignant cerebral edema is the most feared complication of acute ischemic stroke in the setting of covid-19 and in some reports DHE was shown to be life -saving but the mortality is still high [7,11,26,28].

Conclusion

In conclusion, our review reported that acute ischemic stroke is a serious complication in covid-19 cases and it can rapidly cause patient's deterioration by developing malignant cerebral edema. Data about outcome of these patients specially the one who underwent DHS is limited and further studies are needed. Also all clinicians must be familiar with the risk of AIS and its presentation to improve quality of care.

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