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INTRAVENOUS THROMBOLYSIS FOR STROKE IN A COVID-19 POSITIVE PATIENT

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ABSTRACT

The novel coronavirus 2019 (COVID-19) also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an enveloped, non-segmented positive-sense RNA virus belonging to the beta-coronaviridae family [17]. In India, the number of COVID-19 confirmed positive cases is over 22 lacs and is expected to rise [18]. This infection induces a prothrombotic state which can cause acute myocardial infarction and acute ischemic stroke. Here we present a case of a 56-year old male who was admitted with fever, cough, shortness of breath and was COVID-19 positive. He suffered from an ischemic stroke while in the HDU and was given Intravenous thrombolysis with alteplase.

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) is the novel coronavirus first detected in Wuhan, China, that causes coronavirus disease 19 (COVID-19)[1].The past few decades have witnessed deadly epidemics and pandemics caused by COV infections such as the severe acute respiratory syndrome (SARS-COV) and Middle East Respiratory Syndrome Coronavirus (MERS-COV)[2] The pathogenesis of COVID-19 evolves in three phases. In the early infection phase, the inflammatory response is localized to the mucosa of the upper respiratory tract. During this phase, the patient is infected and transmits the disease to others. In the next pulmonary phase, the virus proliferates and invades the lungs. There are lung damage, hypoxemia, and cardiovascular dysfunction. In the last, inflammatory response phase, there is a cytokine storm.[26]Severely infected covid-19 patients might be at risk of thromboembolic events from COVID associated coagulopathy[3,4,5,6] Acute Ischemic stroke was reported during the earlier severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) epidemics[7,5]

Case

A 56 years old male, known hypertensive, presented to the fever opd with history of fever of 8 days duration, cough and shortness of breath of 1 day duration. He was admitted as a case of suspected COVID infection. His routine investigations were done (table 1). Covid-19 nasopharyngeal swab test (RT-PCR) was done on first day of admission which came positive on second day (**Figure 2**). He was started on injectable cefepime + tazobactam 2.25gm TDS, methylprednisolone 40mg BD, low molecular weight heparin 60mg OD, vitamin-c 3gm OD, trace elements OD and oxygen support of (15L via non rebreather mask). During the third hospital day, he developed sudden onset of dysarthria and left upper and lower extremity weakness, with **NIHSS of 6** (facial palsy +1, left arm motor drift +1, left leg motor drift +1, Dysarthria +2). Urgent non-contrast CT Head was done which revealed no intracranial haemorrhage (**Figure 3**). After ruling out any contraindications and a written informed consent from relative, he was thrombolysed withInjection alteplase (0.9mg/kg). A total of 70mg dose was given out of which 7mg was given as bolus and remaining over 60 minutes. Post thrombolysis, his dysarthria improved completely but continued to have left hemiparesis **NIHSS of 2** (left arm motor drift +1, left leg motor drift). Repeat non-contrast CT Head done 24 hours post-IV rTPA showed absence of haemorrhage and **a 1.7 x 1.4cm sized infarct was noted in right parieto-temporal lobe junction in subcortical region (figure 4).** Post thrombolysis, he continued to remain on oxygen support (6L) for respiratory involvement. He developed transient hypotension which was corrected with IV fluids. He was given Tablet Ecosprin 150mg, tablet atorvastatin 40mg and low molecular weight heparin along with antiviral for COVID infection. Over the next 1 week his oxygen requirement decreased and blood pressure stabilised and his left hemiparesis improved completely with **NIHSS of 0**. He was discharged on day 19 of admission on antiplatelet and statin with advice for close follow up.

Table 1 -

Test	Score
WBC	9,000
Lymphocyte Count	15%
NLR	8.8
Platelet Count	4.07
Creatinine	0.85
Lactate Dehydrogenase	444
Prothrombin Time/INR	13.3/1.13
CRP	224.3
ESR	36
D- dimer	1631
Albumin	3.23
ALT	46
AST	22
Imaging Features - Bilateral infiltrates - Consolidation	 - present - present

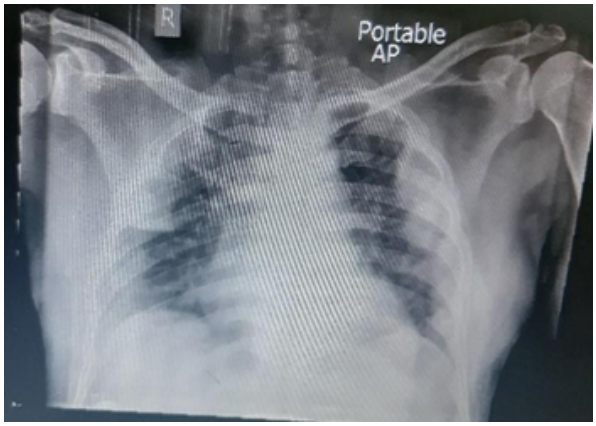

Figure 1 – Chest X-ray

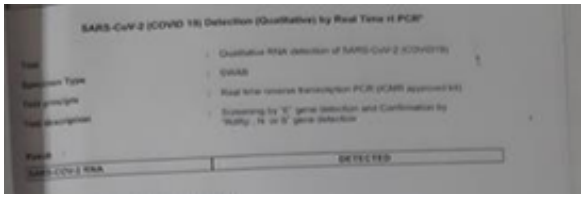

Figure 2 –sars-cov-2 Report

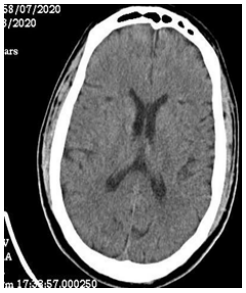

Figure 3 - Non contrast Ct brain Pre Thrombolysis

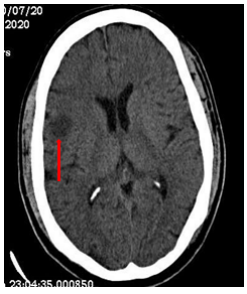

Figure 4 -Non contrast ct brain Post Thrombolysis – Showing 1.7 X 1.4cm Sized Infarct Was Noted In Right Parieto-temporal Lobe Junction In Subcortical Region

DISCUSSION

According to the Health Commission of Hubei province, China, multiple pneumonia cases first appeared in Wuhan with unclear etiology in December 2019 [8,9]. Soon after, a novel type of coronavirus SARS-CoV-2 (coronavirus disease 2019; previously 2019– nCoV) was isolated by Chinese authorities on 7 January 2020 [10,11].

Sars-Cov-2 infects the respiratory tract by inducing release of inflammatory cytokines such as interleukin (IL) 1 band IL-6 by binding to the Toll Like Receptor (TLR), triggering an inflammatory cascade and resulting in Acute Respiratory Distress Syndrome. Suppression of the inflammatory mediators have been shown to limit injury.[15]

Pro-inflammatory cytokines, and in particular interleukin (IL)-1, are important mediators in local and systemic inflammation [13].

Early indicators suggest that cerebrovascular disease in COVID-19 might be due to a coagulopathy. SARS-CoV-2 can cause damage to endothelial cells, activating inflammatory and thrombotic pathways.[19] Endothelial cell infection or monocyte activation, upregulation of tissue factors, and the release of microparticles, which activate the thrombotic pathway and cause microangiopathy, might occur for SARS-CoV-2 as for other viruses.[20,21] Monocyte activation is postulated to constitute part of the secondary haemophagocytic lymphohistiocytosis described in severe COVID-19.[22]

There are several potential explanations for the relation between COVID-19 associated ischemic strokes and increased stroke severity, which may co-exist. It was proposed that viral infections may cause a direct vasculopathic effect (endotheliopathy) or potentiate the prothrombotic milieu via several mechanisms including immune-mediated cardiac arrhythmias.[24] It is unclear whether the finding of increased severity in COVID-19 associated ischemic strokes applies to all ischemic stroke types or is mainly driven by an increase in large-vessel occlusion strokes, as implied by recent findings.[25]

Diagnostic parameters of COVID-19 patients show elevated erythrocyte sedimentation rate, lactate dehydrogenase, C-reactive protein and D-dimer which are seen in our patient (Table 1)

COVID-19 causes a prothrombotic state and can predispose to ischemic events which include cerebrovascular accident, cardiovascular compromise, decreased oxygenation in the setting of acute respiratory distress syndrome and systemic inflammation causing plaque disruption or thrombosis. Studies have confirmed that coronavirus infection can cause myocarditis and even congestive heart failure [12].

There is a retrospective case series on neurological manifestation from China by Mao et al.[23] The various neurological manifestations and complications of COVID-19 are dizziness, headache, acute cerebrovascular disease, impaired consciousness, transverse myelitis, acute hemorrhagic necrotizing encephalopathy, encephalopathy, encephalitis, epilepsy, ataxia, hypogeusia, hyposmia, neuralgia, Guillain barre syndrome, skeletal muscle injury.

There is emerging literature that coronavirus disease of 2019 (COVID-19) infections result in an increase incidence of thrombosis secondary to a prothrombotic state. Initial studies reported ischemic strokes primarily occurring in the critically ill COVID-19 population. However, there have been reports of ischemic strokes as the presenting symptom in young non-critically ill COVID-19 patients without significant risk factors. Further characterization of the COVID-19 stroke population is needed. The duration of the COVID-19 related prothrombotic state is unknown and it is unclear if patient are at risk for recurrent strokes. Due to the variable presentation of COVID-19 ischemic strokes, clinicians can consider neuroimaging as part of evaluation in COVID-19 patients with either acute focal or non-focal neurologic symptoms. Additional studies are needed to clarify prothrombotic state duration and determine prognosis for recovery.

As time is of the essence in ischemic stroke patients, it is important that stroke protocol be followed as per the guidelines It could be secondary to viral infiltration or hypoxia and cytokine storm mounting in response to systemic infection [14] In this case, the patient was thrombolysed within 4.5 hours window period and was managed with antithrombotics and antiplatelets.

CONCLUSION

COVID-19 primarily affects the respiratory and cardiovascular system. However neurological involvement is not uncommon and can result in serious complications if not detected and managed early. These complications are mostly seen in severely ill patients and in some cases can even precede the respiratory symptoms or many be the only symptoms in COVID-19 patients. Therefore, a high index of suspicion is required while dealing with such cases for prompt treatment and prevention. Emergency stroke protocol should be activated in acute stroke cases in covid-19 infection in the same way as for non-covid patients

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