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Cerebral Microbleeds on Susceptibility Weighted Imaging Following Severe COVID-19 Infection

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Abbreviations: MRI: Magnetic resonance imaging; CMB: cerebral microbleeds; SWI: susceptibility weighted imaging; GRE: gradient echo sequence; SARS-COVID: severe acute respiratory syndrome coronavirus

Abstract

COVID-19 infection has known pulmonary involvement but has also been shown to be associated with many neurological manifestations including cerebral microbleeds and leukoencephalopathy. The primary goal of this review is to evaluate the earlier recognition of SARS-COV2 leukoencephalopathy and cerebral microbleeds by MRI brain sequences susceptibility weighted imaging (SWI) versus gradient-echo pulse sequences (GRE) or SWI-minimum intensity projections. Within this paper, we detail two cases that exhibit SWI identifying diffuse cerebral microbleeds in COVID-19 patients. In the first case, SWI imaging was more sensitive and reliable than GRE as follow up imaging with GRE two days after SWI imaging did not identify microbleeds. Prompter identification of these microbleed with an optimal neuroimaging modality such as SWI could lead to earlier treatment therapies and overall improved patient outcomes. In addition, if there was a gold standard neuroimaging modality for cerebral microbleeds, it could be applied to other disease processes such as vascular dementia, cerebral amyloid angiopathy and hypertension.

Keywords: COVID-19; susceptibility weighted imaging, gradient echo sequences; cerebral microbleeds, acuter respiratory distress syndrome; cerebral amyloid angiopathy

Introduction

COVID-19 has known pulmonary involvement, but there is also evidence of neurological manifestations such as leukoencephalopathy and/or cerebral microhemorrhages (CMBs). The pathophysiology of CMB is unknown, but several proposed mechanisms exist as detailed below. Prior studies have evaluated the role of MRI in evaluating CMBs; however, recommendations of which series to utilize have not been fully discussed. Our patient cases demonstrate the superiority of SWI source imaging in diagnosing CMBs.

Case Report #1

A 66-year-old woman without medical history was brought to

the hospital for generalized tonic-clonic seizures and unresponsiveness. On arrival, her temperature was 103.9 degrees Fahrenheit, heart rate was 120 beats per minute and oxygen saturation was 90% on 6 liters via nasal cannula. Polymerase chain reaction testing for COVID-19 was positive. A point-of-care venous blood gas revealed hypercapnia prompting intubation. A lab workup that included thyroid stimulating hormone, complete blood count, comprehensive metabolic panel, ammonia, ethanol level, glucose, urine drug screen and salicylate level was unremarkable.

The patient was admitted to the intensive care unit for acute hypoxic hypercapnic respiratory failure and acute metabolic encephalopathy. She was started on levetiracetam for generalized tonic-clonic seizures, dexamethasone for COVID-19 pneumonia and ceftriaxone, vancomycin, and ampicillin for empiric meningitis coverage. A lumbar puncture was performed with a normal cell count, protein and glucose, negative infectious work-up and negative encephalopathy panel. Computed tomography of her head, chest (with angiography), abdomen and pelvis did not explain her altered mental status or respiratory failure. Due to persistent encephalopathy, MRI brain with SWI sequence was performed, revealing diffuse cerebral microbleeds. Follow up imaging with GRE sequence two days later did not reveal the same lesions seen on SWI. Sputum cultures from a bronchoscopy performed for worsening respiratory function grew aspergillosis. Antifungal therapy with voriconazole was initiated, but her respiratory function continued to decline. Following a lack of improvement in mentation and respiratory status, the family transitioned her to comfort care. Three weeks from admission, the patient expired (Figure 1).

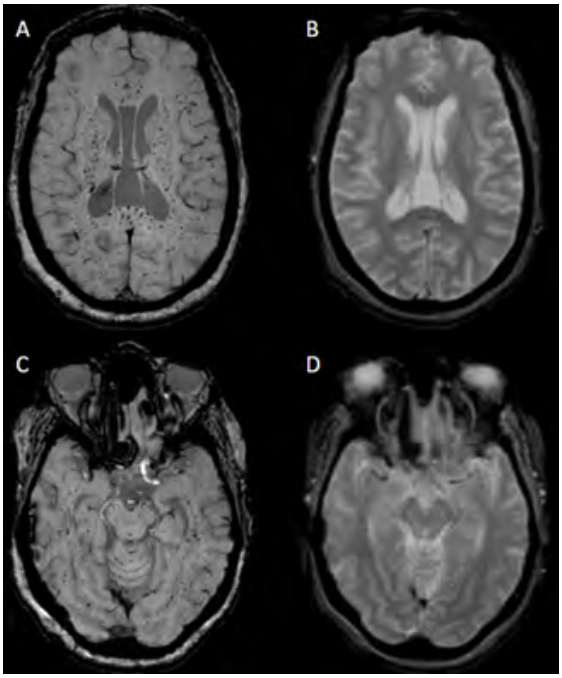

Figure 1: SWI sequence on MRI (A&C) of the 66-year-old female showing numerous supratentorial (A) and infratentorial (C) susceptibility lesions compared to GRE on MRI (B&D) showing no hypointense signal in the brain tissue.

Case Report #2

A 57-year-old unvaccinated woman without pertinent medical history presented to the hospital with dyspnea. Nine days earlier, she had tested positive for COVID-19. Initially hypoxic, her oxygen saturation improved with high-flow nasal cannula. Additional vitals were within normal limits. Troponin, B-type natriuretic peptide, comprehensive metabolic panel and complete blood count were unremarkable. Computerized tomography angiography revealed multifocal ground glass opacities but was without evidence of pulmonary embolism. The patient was admitted and started on intravenous dexamethasone, remdesivir and baricitinib. Over the next two weeks her respiratory status fluctuated, prompting treatment with broad-spectrum antibiotics on two separate occasions. Up to this point, blood cultures and streptococcus and legionella urine antigens were negative.

Three weeks from admission, a rapid response was called for increased oxygen requirements and hypotension. A chest x-ray showed worsening multifocal pneumonia. She was transferred back to the intensive care unit and intubated. Broad-spectrum antibiotics were again started with the addition of voriconazole and valganciclovir and bilateral chest tubes were placed for bilateral pneumothoraxes. Despite these interventions, she later became hypoxic and hypotensive on three vasopressors. Her respiratory status improved with diuresis and blood transfusions for anemia, but she remained unresponsive. On examination, respiratory drive and pupillary response were present but purposeful movements and remaining brainstem reflexes were absent. Non-convulsive status epilepticus was absent on an electroencephalogram. SWI sequence on MRI brain showed innumerable tiny susceptibility lesions throughout the brain. After 32 days with lack of arousal, the decision was made to withdraw life support (Figure 2).

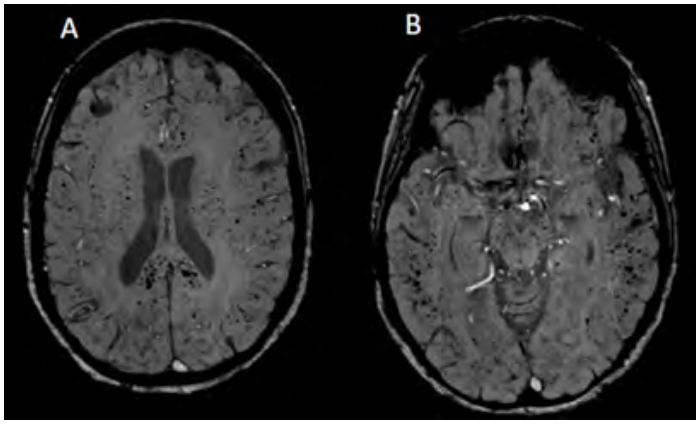

Figure 2: SWI sequence on MRI of the 57-year-old female showing numerous supratentorial (A) and infratentorial (B) susceptibility lesions.

Discussion

SARS-COVID-19 primarily affects the pulmonary system, but neurological manifestations are not uncommon. Reported neurological manifestations include but are not limited to encephalitis, infarct, hemorrhagic stroke, Guillain-Barre syndrome, leukoencephalopathy, seizures, neuropathy, cerebral microbleeds, gustatory and olfactory dysfunction [6]. Investigation into neurological manifestations with neuroimaging is still ongoing. Initial reported neuroimaging findings with COVID-19 included infarct, hemorrhage and encephalopathy [5, 7]. As stated above, leukoencephalopathy and cerebral microhemorrhages continue to be identified in patients with COVID-19.

In one series of 11 critically ill patient with COVID-19 who underwent MRI brain imaging for persistent depressed mentation, four patients had diffuse leukoencephalopathy, one patient had cerebral microbleeds and six patients had both leukoencephalopathy and cerebral microbleeds [5]. The pathophysiology of cerebral microbleeds is unknown but postulated to be multifactorial secondary to hypoxia, a proinflammatory state, hypercoagulability, disruption of endothelial cells and the blood brain barrier [2, 6, 7]. The presence of cerebral microbleeds and/or leukoencephalopathy remains associated with critical illness, worse functional outcome, increased hospitalization, increased morbidity and increased mortality in COVID-19 patients [3]. Earlier recognition of SARS-COV2 leukoencephalopathy and/or cerebral microbleeds could possibly modify and improve patient outcomes. For example, imaging may influence the decision to start anticoagulation given the hypercoagulable state observed in COVID-19 patients [4].

Our patient cases demonstrate the superiority of SWI source imaging rather than GRE or SWI-minimum intensity projections for diagnosing CMBs. In addition to our cases, in the Conklin et al study, MRI brain SWI sequence was used to evaluate sixteen patients with severe COVID-19 because of the optimal sensitivity for detecting microvascular lesions. Eleven of the sixteen patients had punctate SWI lesions in the subcortical and deep white matter, eight patients had more than ten SWI lesions and four patients had lesions involving the corpus callosum. A brain autopsy was performed on one patient with SWI lesions with microvascular injury on autopsy corresponding to imaging findings [4]. Per Agarwal et al, SWI is considered the gold standard for assessing cerebral microbleeds as it has been shown to be more reliable and has a higher detection sensitivity [2]. On detection of CMBs in other diseases such as vascular dementia, SWI was shown to have three advantages over GRE T2. Those advantages were the use of phase information, the high resolution and the long TE which contributed to the increased susceptibility effect. In addition, SWI's sensitivity to hemosiderin, a byproduct of microbleeds, allowed for detection of microbleeds as small as 1mm [1].

In conclusion, based on our case reports along with additional studies, SWI appears to be superior to GRE or SWI-minimum intensity projections for detection of cerebral microbleeds. SWI could thus become the gold standard for detecting cerebral microbleeds in COVID-19 patients along with vascular dementia, cerebral amyloid angiopathy, hypertension and other diseases. CMBs and the hypercoagulable state in COVID-19 infection with an emphasis on anticoagulation recommendations could be a possible area of further investigation.

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