



Case report

Neuro-imaging manifestations of COVID-19: Predilection for PICA infarcts



Manzoor Ahmed^a, Waqar Haider Gaba^{b,*}, Safaa Saeed Al Mazrouei^a

^a Department of Radiology, Sheikh Khalifa Medical City, PO BOX: 51900, Abu Dhabi, United Arab Emirates

^b Department of Medicine, Sheikh Khalifa Medical City, PO BOX: 51900, Abu Dhabi, United Arab Emirates

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ABSTRACT

COVID-19 has been an ever-evolving viral pandemic which can cause systemic disturbance especially in some of the critically ill patients. Neurologic or Neuro-imaging manifestations of COVID-19 are being increasingly reported in these patients and mainly consist of ischemic strokes, hypoxic ischemic injury and non-specific encephalopathy. Ischemic strokes as expected more commonly afflict major vascular territories, likely due to accentuated hypercoagulability in these patients. Certain vascular territories may be more susceptible to ischemic infarcts. We observed higher predilection for infarcts in posterior inferior cerebellar artery (PICA). This may represent another peculiarity of this pandemic.

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Introduction

COVID-19 pandemic has been caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). There is strong association with coagulopathy causing arterial and venous thrombosis [1–4]. The triggering of coagulopathy is linked to alveolar damage resulting in an inflammatory storm. There is activated production of inflammatory cytokines including IL-6 with multi-fold sequential effects particularly generation of pro-coagulative factors and damage to endothelium, which in turn sets up the field for thrombosis and arterial to arterial thrombo-embolism [5,6]. Hence, there is an association of COVID-19 with ischemic stroke, however the pathogenesis is likely multi-factorial rather than merely COVID-related coagulopathy [7] as there is a high incidence of cardiovascular disease or associated co-morbidities (like diabetes and hypertension) in patients with severe COVID-19 [7] and the infection itself has shown to be a risk for stroke even before COVID-19 [8].

The reported cases of ischemic strokes in COVID-19 patients mainly affected medium to large vessels territorial infarcts [9,10] in comparison to more common small vessel ischemic disease in patients with high risk for cerebrovascular disease. Khan et al. [11] recently reported 22 cases of acute ischemic stroke in COVID-19

patients, 18 of them presented with strokes. Majority involved major vascular territories- about 65 % anterior circulation, 27 % posterior & 15 % mixed. However, the overall incidence of stroke in COVID-19 patients has been low- about 5% from one of the study from China [12]. Belani showed COVID-19 as an independent risk factor for stroke [13].

Avula et al. [10] had majority of their cases involving posterior circulation. We also present here 6 out of 9 stroke cases affecting posterior circulation, all these patients turned out to be COVID-19 positive on PCR testing. All these patients had sub-acute infarcts of posterior inferior cerebellar artery (PICA) on imaging. This case series attempts to highlight the predilection for PICA infarcts in COVID-19 cases as well as sub-acute clinical presentation and eventual manifestation during their hospitalized course due to COVID-19. This adds to many peculiarities of COVID-19 as being revealed while we battle this pandemic. Ischemic stroke is one of the many neurologic or neuro-imaging manifestations of COVID-19 [14].

Case series

During the first wave of pandemic in four months, we had 983 patients admitted in our institution, proven positive for COVID-19 on PCR or serologic testing and 9 had evidence of acute or sub-acute infarcts on neuroimaging. Six cases with PICA infarcts were further studied. All cases had initial non-contrast CT head while all except one case had follow up MRI stroke exams to confirm the PICA infarcts. As part of institutional protocol for COVID-19 testing,

* Corresponding author.

E-mail addresses: manahmed@seha.ae (M. Ahmed), wgaba@seha.ae (W.H. Gaba), safalmazrouei@seha.ae (S.S. Al Mazrouei).

Table 1
Demographic, clinical, biochemical and imaging profile of our cases.

Profile	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	62	45	52	41	76	74
Gender	Male	Male	Male	Male	Female	Male
Presentation	Syncope & Fall	Fever, Cough, Confusion	Fever, SOB, Confusion	Syncope & Headache	Fever, Cough & Vomiting	Fever & Cough
Late Onset Stroke symptoms	None	Confusion, Ataxia& dysarthria four weeks later	Ataxia ten days later	None	Confusion& low GCS one week later	Confusion one week later
Co-Morbidities	CAD	None	DM & HTN	HTN	Previous Stroke	DM, HTN, CAD & AF
Serum Ferritin (30–400 mcg/L)	450	1010	1978	247	631	1115
LDH (135–225IU/L)	327	294	324	–	461	1245
D-Dimers (<0.50mcg/mL)	>20	1.2	>20	0.58	3.95	>20
CRP (<5.0 mg/L)	32.5	27	4.8	14.5	100	56.7
Antithrombotic prior to Stroke	Dual Antiplatelet	High dose LMWH	Treatment dose LMWH	None	Prophylaxis dose LMWH	DOAC
Chest Imaging Disease severity	Moderate	Moderate	Severe	Mild	Moderate	Severe
Vascular Territory	PICA	PICA	PICA, MCA	PICA	PICA	PICA, MCA, PCA

CAD: Coronary Artery Disease; SOB: Shortness of birth; DM: Diabetes Mellitis; HTN: Hypertension; AF: Atrial Fibrillation; LDH: Lactate Dehydrogenase; CRP: C-reactive protein. LMWH: Low Molecular Weight Heparin.

almost all patients had available biochemical lab profile as part of standard protocol in our institution. The demographic, clinical and biochemical profile is presented in Table 1. The neuroimaging features of each case are elaborated as below with corresponding figures:

Case 1 (Fig. 1)

Initial CT showed post-traumatic changes due to syncope and fall with bifrontal large contusions in addition to mild intracranial hemorrhage. Follow up CT revealed isolated left PICA sub-acute infarct which was likely the primary cause of patient's fall.

Case 2 (Fig. 2)

Initial CT Head imaging was non-revealing. Follow-up 2 MRI exams confirmed isolated left inferior PICA small sub-acute infarct with petechial hemorrhage. First MRI did raise the possibility of cerebellitis due to potential infectious dissemination of COVID-19.

Case 3 (Fig. 3)

MRI was the initial exam showing well demarcated right medial PICA sub-acute infarct as confirmed on post-contrast imaging. Tiny additional supratentorial embolic cortical infarcts were also present in MCA distribution.

Case 4 (Fig. 4)

Initial ER CT imaging revealed large isolated right PICA hemorrhagic cerebellar infarct with significant vasogenic edema and mass effect in the posterior fossa. The findings on the CT were also suggestive of primary hematoma, hemorrhagic cerebellitis and hemorrhagic neoplasm. MRI confirmed the diagnosis of right PICA sub-acute hemorrhagic infarct.

Case 5

CT imaging demonstrated well-demarcated moderate-sized isolated left posterior superior non-hemorrhagic sub-acute infarct in the PICA distribution. No follow up MRI exam was performed.

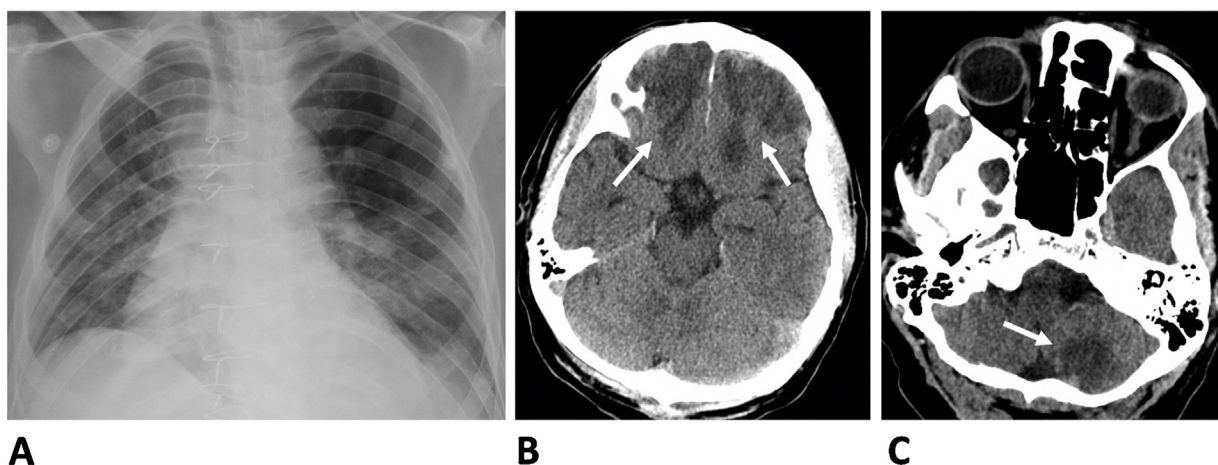


Fig. 1. Frontal chest plain film (A) shows bilateral mid lung zones mild burden of ill-defined patchy but hazy opacities, equivalent to ground-glass changes on High resolution CT Chest. Initial Non-contrast CT Head (B) only demonstrated post traumatic changes of bifrontal large contusions with mild hemorrhage (arrows). Follow-up CT Head (C) demarcating small left PICA sub-acute infarct (arrow) with minimal petechial hemorrhage.

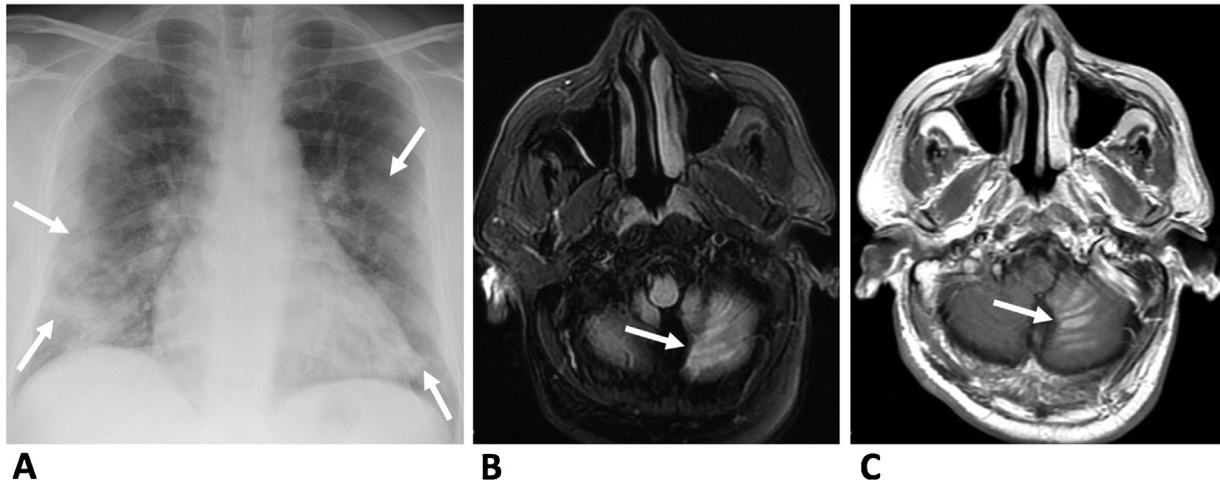


Fig. 2. Frontal chest plain film (A) showing bilateral mid to lung zones moderate burden of ill-defined patchy opacities. Follow-up MRI Brain demonstrates inferior medial left PICA sub-acute infarct (B,C-arrow) with FLAIR T2 hyperintensity of the cerebellar folia (B) and corresponding T1 hyperintensity representing cortical laminar necrosis (C) with out discernible enhancement. No petechial hemorrhage on susceptibility images (not shown).

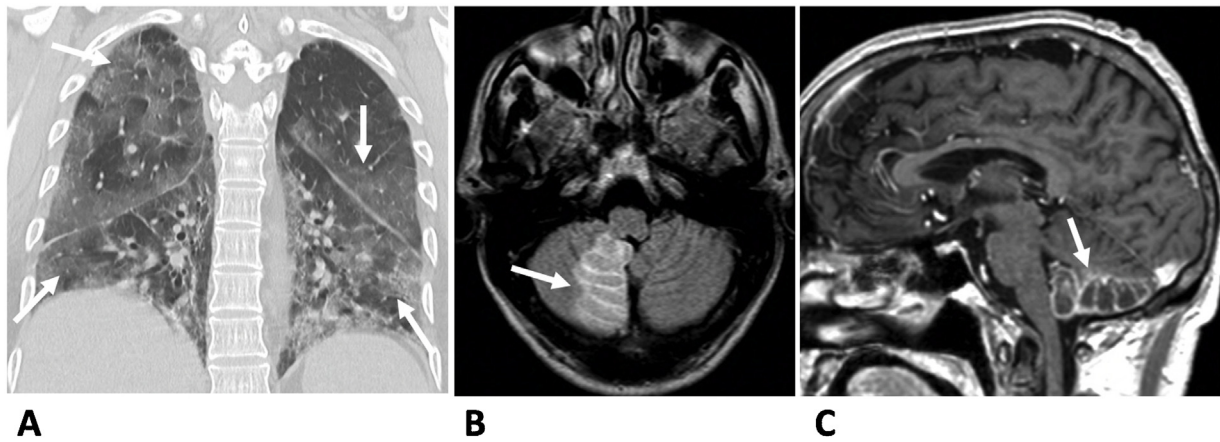


Fig. 3. Coronal CT chest plain image (A) manifests bilateral confluent ground glass changes (arrows)- typical for COVID-19 with severe burden of disease (Score >18). Sub-acute PICA infarct is evident in the right inferior medial distribution with gyriform FLAIR T2 hyperintensity (arrow, B) and corresponding enhancement (arrow, C).

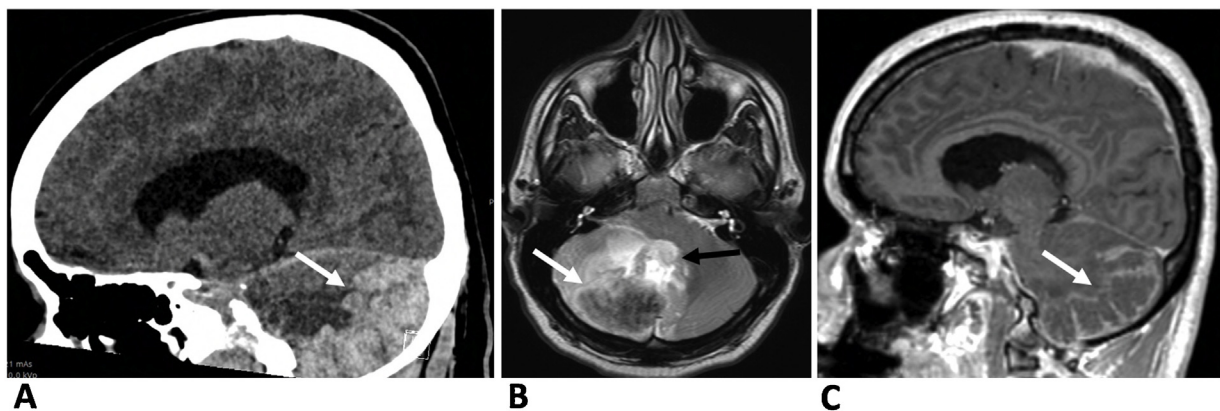


Fig. 4. Sagittal CT showing thick rind of hyper-density(A) in the entire PICA distribution due to hemorrhagic sub-acute PICA infarct with expected vasogenic edema (dark arrow, B) and effaced 4th ventricle due to mass effect. Obstructive hydrocephalus was present (not shown). Note dark T2 signal due to blood products (white arrow, B) and rim enhancement of the sub-acute infarct (arrow, C).

Case 6

Both CT and MR imaging showed multiple sub-acute embolic infarcts of varying sizes in anterior and posterior vascular distribution including bilateral small to moderate sized non-hemorrhagic PICA infarcts.

Discussion

We present a case series of COVID-19 patients with mostly isolated PICA infarcts. Predilection for PICA distribution may be another revealing unique manifestation of COVID-19, a disease which certainly needs more exploration specially its Neurologic Manifestations. COVID-19 as a systemic infectious disorder raise the risk for stroke in these patients with potential to cause altered clinico-imaging presentation, distribution and course of infarcts as somewhat evident from our study. Our cases were focused on cerebellar infarcts in COVID-19 patients.

Large size cerebellar infarcts represent vascular territorial infarcts in PICA, AICA and SCA distribution. The dominant cause of PICA infarcts is also arterial-arterial thrombo-embolism from extracranial large arteries followed by cardio-embolism or in-situ disease [15]. However, hyper-coagulability can certainly contribute to cerebellar infarcts. This can be the potential mechanism in strokes related to COVID-19. In two of our patients, infarcts were large enough to involve more than half of PICA distribution.

PICA is a peculiar vessel due to its tortuous course and high variability in its course [16]. About 10 % of cases have extra-dural origin of PICA [16]. Predilection for posterior circulation infarcts in COVID-19 cases especially PICA distribution can be potentially explained by factors including systemic issues which may be attributed to constitutional effects of COVID-19 including dehydration and hypercoagulability as usually manifested in biochemical profile of these patients, and local factors intrinsic to the vessel as typically seen in atherosclerotic disease. However, anatomical vascular peculiarity and variations can pose a more viable risk to these isolated infarcts. Another explanation can be gravitational effects due to location of the PICA. A counter argument would like to see preponderance of infarcts in PICA distribution in so many other systemic diseases. This can be another mystery of COVID-19 that still needs to be unraveled.

PICA typically supplies the posterior-inferior, posterior and medial surface of the cerebellar hemisphere. The rest of the surfaces are supplied by AICA and SCA. PICA infarcts can involve cerebellar vermis and dorso-lateral medulla including inferior cerebellar peduncle. The patterns of PICA infarcts can also be grossly divided into distribution of medial and lateral branches. Kumral et al. [15] studied cerebellar infarcts and showed about 30 % infarcts in medial branch distribution, 10 % lateral branch, 10 % both medial and lateral branches, 25 % involving superficial or deep water-shed of cerebellar arteries, and 10 % had PICA infarcts along with infarcts in other vertebra-basilar distribution. Though cerebellar infarcts constituted only 2% of all the infarcts, but about half of the cases had isolated PICA infarcts suggesting its higher predisposition to infarcts and may be further accentuated by COVID-19. All our cases had posterior-inferior and or medial distribution without brainstem involvement. The infarcts were demarcated on CT due to sub-acute onset.

The sub-acute features of infarcts were also manifested on MRI as mixed restriction diffusion, cortical laminar necrosis, hemorrhagic change and or enhancement. Posterior circulation infarcts are prone to present clinically late as sub-acute infarcts usually due to non-specific symptoms [17]. Some of the infarcts also had associated cerebellar vasogenic edema and surface hyperintensity on FLAIR images mimicking cerebellitis (Fig. 4), inflammatory process can be a plausible differential diagnosis in the setting of

COVID-19 and may even be contributing to relative atypical appearance of the infarct.

Beyrouti et al. [9] described a link between ischemic stroke and COVID-19 infection in the context of a highly prothrombotic state. We observed similar phenomenon in our cases where all patients had positive D-dimers and 3 out of 6 had values >20mcg/mL while 4 out of 6 patients had ischemic stroke despite being on prophylactic or full dose anti-coagulation. Incidentally, all these four patients had late presentation of stroke during the course of COVID-19 disease.

Cases with presentation or detection of cerebral or cerebellar infarcts during hospital course can be plausibly attributed to systemic effects of COVID-19. However, patients primarily presenting with ischemic strokes certainly raise the possibility of coincidence with COVID-19 given its pandemic status in the community. The peculiarity of these cases, especially manifestation, on neuroimaging does lend an attributive if not causative role to COVID-19. As noted above, about 80 % of the cases presented as ischemic strokes in one of the recently reported study [11].

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Consent

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Ethical approval

Local Ethics committee and IRB approval taken.

Author contribution

MA initiated the idea of manuscript, did data analysis and wrote the manuscript. WHG did data collection, data analysis and helped in writing the final manuscript. SA helped in analyzing data, data collection and writing.

Declaration of Competing Interest

The authors report no declarations of interest.

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