Neurological symptoms described in COVID-19 infected patients (hypo-ageusia, anosmia, confusion, seizures, etc.) are often associated to presence of stroke and/or brain hemorrhages that sometimes can occur together. As COVID-19 has spread around the world, evidence has grown for an association with cerebrovascular disease. The association between COVID-19 and cerebrovascular complications were reported in an early retrospective case series from Wuhan [1], Italy [2, 3], and Netherlands [4] and extensively reported in Chap. 2.

The reported incidence of cerebrovascular disease in patients testing positive for SARS-CoV-2 ranges from 1% to 6%, potentially equating to large numbers of individuals as the pandemic progresses in some countries [5, 6], and multiple regions with high COVID-19 prevalence have reported stable or increased incidence of large vessel stroke and increased incidence of cryptogenic stroke (patients with no found typical cause of stroke).

Moreover the mean patient age in several thrombectomy case series of COVID-19 is younger than the typical population having this procedure [7–9], and case-control analysis of acute stroke protocol imaging from late March to early April, 2020, across a large New York City health system showed that, after adjusting for age, sex, and vascular risk factors, SAS-CoV-2 positivity was independently associated with stroke.

Some hypotheses have been postulated to explain cerebrovascular involvement in this infection.

The ACE1-Angiotensin II system is more active in the elderly males and this might explain why increasing mortality and cerebrovascular complications are observed more often in these patients [10, 11].

Early indicators suggest that another process linked with these cerebrovascular complications is the onset of a sepsis-induced coagulopathy (SIC), precursor of disseminated intravascular coagulation (DIC), due to an uncontrolled cytokine release [12]. Endothelial damage and thrombogenic-hemorrhagic processes are compounded by SARS-COV2 neurotropic and neuro invasive ability [13], demonstrated on other strains of human coronavirus in the past [14]. The alteration of coagulability resulted confirmed by the effectiveness of anticoagulant therapy with heparin or rTPA [15].

Lower levels of lymphocytes, platelet count, and higher blood urea nitrogen were also found in patients with CNS symptoms. No laboratory
differences were found between patients with stroke or cerebral hemorrhage.

From an imaging point of view, no peculiar aspects, helpful to discriminate cerebrovascular complications of COVID-19 from classical stroke clinical presentation, were reported at the moment.

Therefore, for this reason arterial and venous imaging evaluation is essential for COVID-19 patients with acute cerebrovascular events, keeping in mind that data supporting an association between COVID-19 and stroke in young populations without typical vascular risk factors, at times with only mild respiratory symptoms, are increasing.

Numerous studies in the literature have investigated the correlation between stroke and cardiovascular and inflammatory events during COVID-19 infection.

Cardiac involvement with acute cardiac injury, arrhythmias and heart failure in COVID-19 patients has been described [16–18]. A meta-analysis of six studies observed cardiac injury in 8.0% patients, mostly occurring in patients who were sicker and in the ICU [19]. The hypothesized mechanisms, including an acute inflammatory response and plaque destabilization, could potentially lead to a cardioembolic stroke.

The relationship between inflammation and stroke is complex because the inflammation could precede, causing it, the stroke, or follow it [20, 21]. The interaction between inflammatory cells within the vascular wall and conventional risk factors alters the dynamics of atherosclerosis. This has a potential to acutely worsen in the presence of systemic inflammation and effect the coagulation cascade [22, 23].

In reference to risk factors the literature data suggest age and comorbidities like hypertension, diabetes and cardiovascular disease to be associated with higher mortality in COVID-19 [18, 24, 25]. In particular a report of patients with COVID-19 and stroke emphasizes coexistence of history of smoking (38.5%), alcohol intake (15.4%), and increased blood pressure (≥130/80 mmHg) (53.8%) [26].

Moreover, patients with stroke were more likely to have other underlying disorders, including hypertension (69.2% vs. 22.1%, \( p < 0.001 \)) and diabetes mellitus (46.2% vs. 12.0%, \( p < 0.01 \)) [28]. A report from the Chinese Center for Disease Control and Prevention describes a significantly higher mortality rate in patients with hypertension, diabetes and CVD (6%, 7.3% and 10.5%, respectively, versus an overall rate of 2.5%) among 44,672 COVID-19 cases. Some more details about cardiac involvement will be summarized in Chap. 6 (Other possible location of Cov-19 infection).

From an interventional neuroradiological point of view, the treatment of stroke does not differ based on the presence or absence of COVID-19 infection.

However, stroke management can be challenging as it involves the need to harmonize the “time is brain” concept and the safe and effective management of the potential spreading source of the virus. The triage processes during needs to ascertain whether the patient is a COVID suspect and delineate pathways for timely treatment and minimum exposure to health care personnel. The organization and management of the out-of-hospital territorial emergency must consider both the number of confirmed infections and the organizational capacity of structures not ready to manage stroke. Similarly, the hospital organization will have to consider adequate logistical and structural changes. Guidelines to manage patients with acute stroke during COVID-19 have been published [27, 28], giving more and more importance to the concept of “protected stroke code.”

As discussed above, one of the supposed pathogenetic mechanisms in COVID viral infection is coagulopathy induced by a proinflammatory state.

This aspect should be considered when dealing with hemorrhagic manifestations of stroke. Discussions regarding anticoagulation for COVID-19 patients have been intensifying as evidence of hypercoagulability in this population continues to accumulate. Recent literature findings can be helpful in this regard. In a cohort of 755 patients diagnosed with positive COVID-19 and with neuroimaging, 4.4% had ICH [29]. The majority of these patients received therapeutic anticoagulation, most commonly UFH. The most
frequent indication for starting anticoagulation was elevated D-dimer levels, reflecting what is indicated by the literature data.

In our center, from March to May 2020, we evaluated a cohort of 205 COVID+ patients. All underwent at least one brain CT. Forty-five underwent a brain CT angiography and 50 a brain MRI (50% of these on 3 T Magnet). Forty percent (79/205) of the brain CTs showed pathological changes; in particular among these 33% showed lobar infarcts, 37% lacunar infarct, and 35% hemorrhagic stroke. On MRI we registered a recurrent pattern of ischemic and/or haemorrhagic lesions in 50% of patients.

### 3.1 Clinical Cases

**Case 1**  F, 63 years old. Acute onset of severe dyspnea associated with confusion, diplopia and speech difficulties. In the previous days she reported fever and flu-like symptoms. \( \text{FpO}_2 \) values between 85% and 89% (Figs. 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, and 3.8).

**Fig. 3.1** Axial CT scan images show a point-like hyperdensity at the apex of the basilar artery. The tomodensitometric values in the posterior cranial fossa do not show alterations of suspected acute ischemic or hemorrhagic significance.

**Fig. 3.2** CT angiography study. Multiplanar MIP reconstructions show thromboembolic defect at the apex of the basilar artery in sagittal, axial and coronal planes. The opacification defect involves the P1 tract of the posterior cerebral arteries and the emergence of the superior cerebellar arteries.
Fig. 3.3 Digital subtraction angiography. Superselective catheterization of the left vertebro-basilar arterial axis demonstrates and confirms the thromboembolic defect at the apex of the basilar artery (a, b). The mechanical thrombectomy procedure led to recanalization of the arterial axes (c).

Fig. 3.4 Contrast enhanced chest CT. The investigation shows multiple filling defects at the level of the main branches of the pulmonary arteries, bilaterally. Findings compatible with pulmonary thromboembolism. The absence of dilation of the right heart cavities suggests an acute onset. After 24 h, due to the sudden onset of left hemiplegia a CT scan is performed.

Fig. 3.5 Axial CT scan does not show tomodensitometric changes referable to ischemic or hemorrhagic lesions. There is only a slight minor representation of the cortical sulci on the left.
**Case 2** Male, 61 years old. Dyspnea and fever for 5 days; presenting with dysarthria. SWAB+; Chest CT+ (Fig. 3.9).

**Case 3** M, 55 years old. Rapid onset of acute headache associated with right hemi syndrome. Upon arrival in the emergency room, relatives report behavioral changes in the previous days (Figs. 3.10, 3.11, and 3.12).

**Case 4** M, 63 years old. Gradual onset of headache. Patient arrives to the emergency room on his
own after about 2 days of symptoms. Fever and mild dyspnea are associated, with FpO₂ values between 95% and 97% (Figs. 3.13, 3.14, and 3.15).

Case 5  F, 69 years old. The patient is taken to the emergency room by an advanced rescue vehicle due to the sudden appearance of dysarthria and dizziness (Figs. 3.16, 3.17, 3.18, and 3.19).

Case 6  F, 62 years old. Recent history of hospitalization for fever and dyspnea. Finding of COVID-19 related pneumonia. Following onset of unclear neurological symptoms, brain CT is performed (Figs. 3.20, 3.21, 3.22, and 3.23).

**Case 6: ex-post re-interpretation:** the lack of complete clinical information due to the peculiar moment of the pandemic, the execution of the first CT scan not in the proper acute phase of the neurological symptoms made difficult the correct definition and classification of this case. As a matter of fact, the actual revision of imaging opens a differential diagnostic issue versus PRES or PRES like classification. We consider this case here as a “vascular” case because it has been classified and treated as vascular; furthermore, we are conscious of possible different interpretations such as PRES like lesion.
Fig. 3.10 Axial CT scan image (on right) and axial angio-CT scan image with MIP reconstruction (on the left) show temporal hemorrhagic lesion with no vascular ischemic alteration on the CT angiogram. This kind of hemorrhage is atypical for location in absence of any vascular pathological findings.

Fig. 3.11 Axial MRI. DWI ($b$-value: 1000) shows restriction into left temporal hemorrhagic lesion with surrounding edema (a) with a correlated ADC map showing restriction into left temporal hemorrhagic lesion with surrounding edema (d). Axial FLAIR (b, c) and Axial T2w (e) show left temporal hemorrhagic lesion with peripheral edema. (f) Axial SWI. Left temporal hemorrhagic lesion. Widespread hypointense changes can be seen at the site of the lesion. This finding is suggestive for the presence of hemosiderin deposits deriving from hemoglobin catabolism and from slow blood flow.
**Fig. 3.11** (continued)

**Fig. 3.12** Angio 3D Tof MIP reconstruction (a) shows no vascular malformations or lesions. Venous phase angio MRI (b): Left sigmoid sinus thrombosis

**Fig. 3.13** Axial CT scan images show temporo-occipital hypodense lesions with hyperdense hemorrhagic alterations and perilesional edema. These findings are compatible with hemorrhagic transformation of the ischemic lesion. Uncertain ischemic hypodensity is also visible at the temporal and occipital-parietal right lobes.
Fig. 3.14 Axial MRI. DWI ($b$-value: 1000) shows inhomogeneous hyperintense left temporo-occipital area of restricted diffusion. This finding is correlated with hypointensity ADC map.

Fig. 3.15 Axial Flair. Left temporooccipital inhomogeneous ischemic lesion.
Case 7  F, 77 years old. Right hemiparesis. Fever and dyspnea of mild onset rapidly progressing are associated (Fig. 3.24).

Case 8  F, 82 years old. History of previous ischemic stroke. Acute appearance of aphasia and confusion. Fever and severe dyspnea (Figs. 3.25 and 3.26).

Case 9  M, 67 years old. Very rapid onset of severe dyspnea associated to Progressive neurological deterioration and coma (Figs. 3.27 and 3.28).

Case 10  M, 66 years old. Acute right hemisindrome dx: during the various attempts at thrombectomy, thrombi continue to be created due to the state of hypercoagulation make the procedure really difficult (Figs. 3.29, 3.30, 3.31, 3.32, 3.33, and 3.34).

Fig. 3.16  Axial CT scan image shows ischemic hypodensity at the superior part of the left cerebellar hemisphere, SCA vascular territory, with dimensional reduction of the cerebellopontine cistern due to conspicuous perilesional edema.

Fig. 3.17  Axial MRI. DWI ($b$-value: 1000) shows restriction at the superior part of the left cerebellar hemisphere, SCA vascular territory with a correlated ADC map.
Fig. 3.18 Coronal T2w scan. Hyperintensity of the superior cerebellar hemisphere (a, b). Axial FLAIR (c, d) shows a perfect overlap of anomalous signal hyperintensity
Fig. 3.19  Axial T2*w. The “blooming effect” in the context of the cerebellar lesion is highlighted

Fig. 3.20  Axial CT scan images show cortical-subcortical hypodensity in both parietal lobes with no hemorrhagic lesions. Findings were defined as compatible with bilateral ischemic lesions
Fig. 3.21  Axial FLAIR shows hyperintense biparietal quite symmetrical lesions predominantly in subcortical region

Fig. 3.22  Axial T2w. The same lesions (Fig. 3.21) can be seen as hyperintense changes with relative sparing of cortical regions. No further alterations of suspected ischemic significance are detectable
**Fig. 3.23** Axial contrast enhanced T1w (a) shows a brilliant “gyral” enhancement associated to a focal T2* hypo intensity (b) suggestive for the presence of hemosiderin deposits deriving from hemoglobin catabolism.

**Fig. 3.24** Axial CT scan (a, b) shows the presence of left nucleus-capsular hematoma associated with a conspicuous area of peri lesional edema. (c) The finding is associated with chest X-ray showing the presence of signs referable to accentuation of the interstitial texture in a patient with a clinical suggestive of COVID-19 related interstitial pneumonia.
**Fig. 3.24** (continued)

**Fig. 3.25** Axial CT scan shows right capsule-thalamic-lenticular hemorrhagic collection, with minimal perilesional edema and blood flooding of the right lateral ventricle, of the third and fourth ventricles. Left deviation of the pellucid septum. Concomitant presence of extensive hemispheric infarct outcomes on the left
Fig. 3.26 Chest X-ray showing the presence of signs referable to accentuation of the interstitial texture in a patient with a clinical suggestive of COVID-19 related interstitial pneumonia. There is no evidence of focal parenchymal thickening or signs uniquely referable to volume overload of the pulmonary circulation.

Fig. 3.27 Axial CT scan shows a diffuse supratentorial cerebral edema and diffuse cerebral parenchymal hypodensity. There is cortical sulci effacement and the difference between white and gray matter is no longer present. The presence of intraparenchymal aerial components of unknown etiology is highlighted.
Fig. 3.28 Serial chest X-ray (a) shows worsening of the pulmonary radiographic picture with the appearance (b) of accentuation of the interstitial texture in a patient with a clinical suggestive of COVID-19 related interstitial pneumonia. The relief is also associated with the appearance of more compact parenchymal thickening in the right lung and reduced lung capacity.

Fig. 3.29 Axial CT scan (a) image show point-like hyperdense left proximal middle cerebral artery (M1-M2 segment). Axial CT scan images (b, c) shows low density area effacing left insular ribbon and slight minor representation of the cortical sulci on the left.
Fig. 3.30 Chest X-ray showing radiological signs referable to accentuation of the interstitial texture in a patient with a clinical picture suggestive of COVID-19 pneumonia.

Fig. 3.31 CT angiography multiphase study; MIP reconstructions show the thromboembolic defect at left proximal cerebral (M1-M2) medial artery (a, b); and bad collateralization; avascular fronto-temporal area in the late phase of CT angiogram (b, c).
Fig. 3.32  Contrast enhanced chest CT. The investigation shows the presence of multiple filling defects at the level of the secondary branches of the right pulmonary arteries. Findings compatible with pulmonary thromboembolism.

Fig. 3.33  Digital subtraction angiography. Super selective catheterization of the left internal carotid artery demonstrates occlusion of the middle cerebral artery at the M2 segment (a). The thromboembolic defect causes the complete absence of the cerebral parenchymography of the corresponding vascular territory (b) and (c) images with occlusion also the distal (A2-A3 segment) left anterior cerebral artery. Multiple successive attempts of recanalization through mechanical thrombectomy failed.
Fig. 3.34 Axial CT scan shows diffuse left hemispheric brain edema-cerebral parenchymal hypodensity as for extensive left infarct in middle and anterior cerebral artery’s territories

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