Neuroimaging Findings in Conjunction with Severe COVID-19

Neuroradiologische Befunde im Zusammenhang mit schwerer COVID-19-Erkrankung

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ZUSAMMENFASSUNG

Ziel COVID-19 hat einen variablen, aber gut beschriebenen klinischen Verlauf. Einige Patienten weisen auch neurologische Symptome auf. Erste Studien zeigen, dass die Erkrankung zu pathologischen Befunden in der neuroradiologischen Bildgebung führen kann. Ziel dieser Studie war die Evaluation von Häufigkeit und Art pathologischer neuroradiologischer CT- und MRT-Befunde in einer großen Kohorte SARS-CoV-2-positiver Patienten als Momentaufnahme in einem Level-I-COVID-19-Versorgungszentrum.

Material und Methoden Es wurden retrospektiv zerebrale CT- und MRT-Aufnahmen von 34 hospitalisierten COVID-19-Patienten in unserem Level-I-COVID-19-Versorgungszentrum zwischen dem 15. März und 24. März analysiert. Zusätzlich zu den radiologischen Befunden wurden auch klinische Parameter wie neurologische Symptome, Komorbiditäten und Art der Beatmungstherapie dokumentiert. Es wurde eine deskriptive statistische Analyse durchgeführt.

Ergebnisse Pathologische Befunde wurden bei 38,2 % der Patienten der Studienkohorte festgestellt. Basierend auf den hausinternen Prävalenzerhebungen zu den SARS-CoV-2 positiv getesteten Patienten zum Zeitpunkt der Datenerhebung konnten bei 6 % aller Patienten (34/565) pathologische Befunde in der Bildgebung festgestellt werden. Die häufigsten Befunde waren Mikroblutungen (20,6 %) und Anzeichen einer hypoxischen Hirnschädigung (11,8 %). Darüber hinaus wurden kortikale Subarachnoidalblutungen, typische und atypische Hirnblutungen, ischämische Schlaganfälle und generalisierte Hirnödeme dokumentiert. Alle pathologischen Befunde traten bei Patienten auf, die entweder intubiert oder mit ECMO behandelt wurden.

Schlussfolgerung Basierend auf der Analyse dieser großen Kohorte SARS-CoV-2-positiver Patienten scheinen pathologische Befunde in der bildgebenden Diagnostik insgesamt relativ selten zu sein. Sie treten jedoch in einem substanziellen Teil der Patienten mit schwerem COVID-19-Krankheitsverlauf auf, die eine Intubation oder ECMO benötigen.

Kernaussagen:

- Pathologische Befunde in der Neurobildgebung sind bei SARS-CoV-2 positiven Patienten relativ selten.
- Pathologische Befunde treten hauptsächlich bei Patienten mit schweren, intensivpflichtigen COVID-19 Verläufen auf.
- Es dominieren hämorrhagische neben ischämischen und hypoxischen Veränderungen.
- Bei Patienten mit schwerem COVID-19 Verlauf sollte niederschwellig eine Neurobildgebung durchgeführt werden.

ABSTRACT

Purpose COVID-19 has a variable, but well-described course. However, some patients additionally present with neurological symptoms. Recent studies also show a broad range of neuroimaging features. The purpose of this study was to perform a snapshot analysis to approximate the frequency and types

of neuroimaging findings on CT and MRI scans in a large cohort of SARS-CoV-2-positive patients in a level I COVID-19 center, both in general and in critically ill patients.

Materials and Methods We retrospectively analyzed brain CT and MRI scans of 34 hospitalized COVID-19 patients at our level I COVID-19 center between March 15 and April 24 with regard to pathological neuroimaging findings. In addition, clinical parameters such as neurological symptoms, comorbidities, and type of ventilation therapy were also documented. A descriptive statistical analysis was performed.

Results Pathological findings were detected in 38.2 % of patients in the study cohort. Based on the weekly institutional SARS-CoV-2 report of all positively tested patients in our clinic at the time of data collection, neuroimaging findings could be found in 6 % of all patients (34/565). The most common findings were microbleeds (20.6 %) and signs of hypoxic brain injury (11.8 %). Furthermore, cortical subarachnoid hemorrhage, typical and atypical cerebral hematomas, ischemic strokes, and generalized brain edema were documented. All neuroimaging findings occurred in patients who were either intubated or treated by ECMO.

Conclusion Based on the analysis of this large cohort of SARS-CoV-2-positive patients, pathological neuroimaging findings seem to be relatively rare in general but do occur in a substantial proportion of patients with severe COVID-19 disease needing intubation or ECMO.

Key Points:

- Neuroimaging findings appear to be relatively rare in SARS-CoV-2 positive patients.
- Pathological findings occur mainly in critically ill COVID-19 patients.
- Frequent findings include hemorrhagic, ischemic and hypoxic changes.
- Critically ill COVID-19 patients should receive neuroimaging with a low threshold.

Citation Format

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Purpose

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak started in Wuhan, China and has rapidly spread around the globe resulting in a pandemic [1, 2]. Most patients with coronavirus disease 2019 (COVID-19) present with cough, dyspnea, fatigue, myalgia, or diarrhea [1]. However, the clinical course is very variable and ranges from asymptomatic patients to severe cases necessitating ventilation or extracorporeal membrane oxygenation [3]. The infection is estimated to follow a severe course in 3–6 % of cases [4, 5]. Meanwhile, studies show that COVID-19 can also cause neurological symptoms. Some patients are even thought to present primarily with neurological symptoms [6]. Recent studies also describe a broad range of neuroradiologic features, like leukoencephalopathy and microhemorrhages 2 [7–11].

In summary, we wanted to perform a snapshot analysis to approximate the frequency and types of neuroimaging findings on CT and MRI scans in a large cohort of SARS-CoV-2-positive patients in a level I COVID-19 center, both in general and in critically ill patients.

Materials and Methods

This retrospective study was approved by the Local Ethics Committee of our hospital (A4/074/20). At the time of data acquisition (April 24, 2020), a total of 565 patients were being treated in our hospital due to COVID-19 disease (based on our institutional daily SARS-CoV-2 report). We have recorded all patients with suspected SARS-CoV-2 infection receiving brain CT and MRI acquired between March 15 and April 24 at our level I COVID-19 center consisting of three academic campuses (n = 98). The indication for unenhanced brain CT was partly based on the hospital's internal guidelines for patients suspected of having SARS-CoV-2 infection. Patients with Glasgow Coma Scale below 15 or a non-apoplectic neurological deficit were to receive unenhanced cerebral CT in combination with unenhanced chest CT. However, some examinations were also performed due to clinical routine indications, e. g., focus search, pre-extracorporeal membrane oxygenation (ECMO) therapy, or for follow-up (a summary of the indications for the cerebral imaging is shown in ▶ **Table 1**). MRI examination were performed as follow-up imaging or for further diagnosis (n = 8). The MRI protocols included the following sequences: T1-, T2-, (fluid attenuated inversion recovery) FLAIR-, diffusion-, susceptibility- /T2*-weighted scans in all cases and MR angiography (time-of-flight) (7/8 cases) as well as contrast-enhanced T1-weighted scans in 8 cases (8/8 cases). A total of 34 patients were included in the study (8 female patients, median age 54 years (range 35–80 years); and 26 male patients, median age 68 years (range 7 months to 82 years)). In addition, comorbidities, neurological symptoms, and the ventilation mode of the patients were recorded from electronically stored patient data.

All investigations were double-read, once during clinical routine by the responsible board-certified consultant neuroradiologists (HCB, AT, BG, with 18, 22 and 34 years of neuroimaging experience, respectively,) and, for study purposes, by another board-certified neuroradiologist (ES) with more than 13 years of experience. Disagreement was resolved by consensus.

Descriptive statistical analysis was performed (LB) using SPSS version 24 software (IBM, Armonk, NY) for Windows version 10 (Microsoft, Redmond, Washington). Absolute and relative frequencies for categorical variables and median and standard deviation for continuous variables are reported in the total study population as well as in the subgroups of patients with and without neuroimaging findings. Since only descriptive statistics were performed, p-values were not given.

▶ **Table 1** Summary of the indications for cerebral imaging in COVID-19 patients.

▶ **Tab. 1** Zusammenfassung der Indikationen für die zerebrale Bildgebung.

Imaging indication according to imaging request form	n (34)	%	Symptoms/clinical features
Rule in/out structural lesions in patients with GCS 15	3	8.8	Focal neurological deficit (hemiparesis, aphasia, vertigo; 3)
Rule in/out structural lesions in patients with < GCS 15 (4) or intubation (17)	21	61.8	COVID-19 infection-, critical illness-, or therapy- associated encephalopathy (7), prolonged wakeup reaction (4) or weaning (2), signs of hypoxic brain injury/post-resuscitation status/oxygen desaturation (8)
Infectious focus screening	8	23.5	Uncontrollable fever (1), elevated infection parameters (5), sepsis (2)
Seizures	1	2.9	
Miscellaneous (post-OP control of a CSF shunt unrelated to COVID19)	1	2.9	

Results

Patient Population

The study population consisted of 34 hospitalized COVID-19 patients with cerebral MRI or CT imaging (26 men, 8 women; median age 67.5 years +/– 17.6 years). Our hospital provides the highest level of care for SARS-CoV2-positive patients (level I COVID-19 center). Due to this fact, most patients were transferred from peripheral hospitals because of severe symptoms (64.8 %, n = 22; median age 60 years). Fewer patients presented themselves to our emergency department (17.6 %, n = 6; median age 68.5 years) or were brought to our institution by rescue service (17.6 %, n = 6; median age 77.5 years). 84.4 % patients had to be transferred to the intensive care unit (ICU). The median time interval from the onset of symptoms to intubation was 6.5 days (see ▶ **Table 2**).

Patients with pathological neuroimaging findings were more often younger and had a more severe course. Those patients required invasive ventilation and extracorporeal membrane oxygenation (ECMO) more frequently. There was no difference between patients with and without abnormal findings in terms of comorbidities. 47.1 % of all patients had recorded acute neurological symptoms. Cerebrospinal fluid analyses were only infrequently (n = 5) performed. Patients with positive neuroimaging findings had more frequent neurological symptoms, especially disturbances of consciousness (see ▶ **Table 2**).

Imaging Findings

From the cohort, 13 patients (38.2 %) showed brain imaging abnormalities either on initial or follow-up brain imaging. Clinically irrelevant incidental findings were found in 4 patients (not further counted), and 17 patients had normal scans. Based on our institutional weekly SARS-CoV-2 report of all positively tested patients in our clinic at the time of data collection, neuroimaging findings could be found in 6 % of all patients (34/565).

All patients with pathological findings were already intubated or oxygenated by ECMO at the time of the CT/MRI examination or eventually needed to be in the course of a severe disease. 26.5 % patients showed hemorrhagic manifestations (n = 9), most commonly microbleeds (20.6 %, n = 7), followed by focal sulcal convexity subarachnoid hemorrhage (11.8 %, n = 4), superficial hemosiderosis of the convexity (8.8 %, n = 3), loco typico hematoma (2.9 %, n = 1) and lobar hematoma (2.9 %, n = 1). Signs of hypoxic brain injury were found in 4 patients (11.8 %). In two patients acute or early subacute ischemic stroke was seen (5.9 %) (one cortical and one subcortical). One patient showed generalized brain edema (2.9 %). A synopsis of imaging findings is shown in ▶ **Fig. 1–3**.

Conclusion

The main findings of this snapshot analysis investigating a large cohort of COVID-19 patients regarding frequency and types of neuroimaging findings are that only 34 of 565 patients (6 %) treated in our level I COVID-19 center required neuroimaging based on the hospital guidelines or routine indications (ECMO, etc.). However, 13 of these 34 patients (38.2 %), all of whom were intubated or oxygenated by ECMO, had abnormal findings. Furthermore, 12 of the 34 patients with intubation and ECMO had no neuroimaging findings. It therefore seems reasonable to conclude from our data that pathological neuroimaging findings are relatively rare in the general COVID-19 population but do occur in a relevant subset of severe COVID-19 patients needing advanced respiratory therapy.

COVID-19 has a variable and emerging clinical phenotype and has recently been shown to also cause neurological symptoms [3]. Consistent with the findings of Mao et al., neurological symptoms, such as reduced consciousness, were more frequent in patients with severe infection [6].

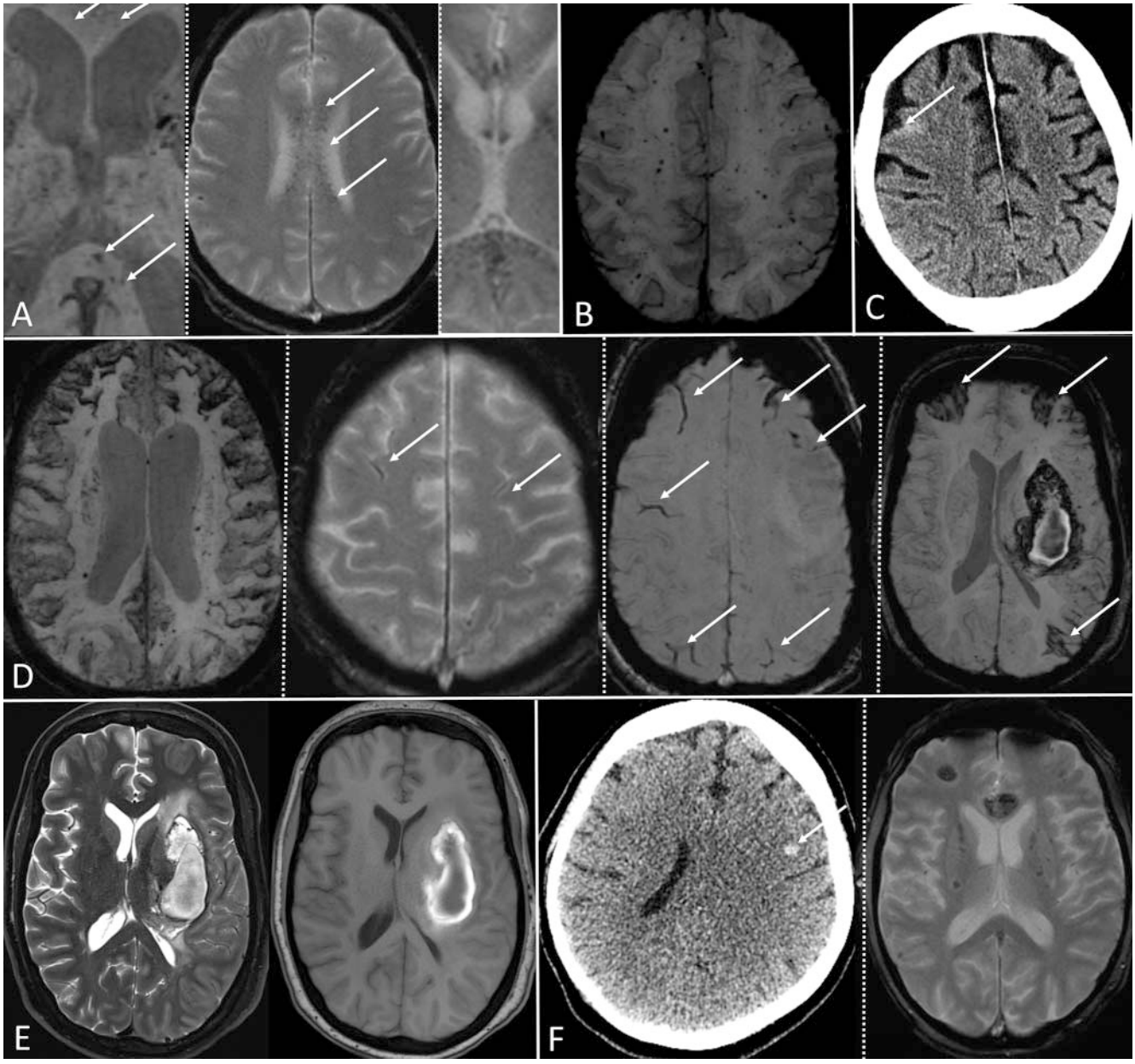
Pathological neuroimaging findings in COVID-19 patients might either result from direct viral effects on the brain or secondary effects in connection with pulmonary disturbances (e. g., hypoxia secondary to COVID-19 pneumonia and ARDS) or from treatment effects (e. g., invasive ventilation, ECMO, or various medications) as well as a combination of these factors. As our understanding of the disease and its pathomechanisms is currently still limited, a definite differentiation of damage patterns is difficult.

▶ **Table 2** Summary of demographic and other patient data in the whole cohort and stratified by imaging findings. ECMO – extracorporeal membrane oxygenation. ICU – intensive care unit.

▶ **Tab. 2** Zusammenfassung von demografischen und anderen Patientendaten in der gesamten Kohorte und gegliedert nach bildgebenden Befunden. ECMO = extrakorporale Membranoxygenierung; ICU = Intensivstation.

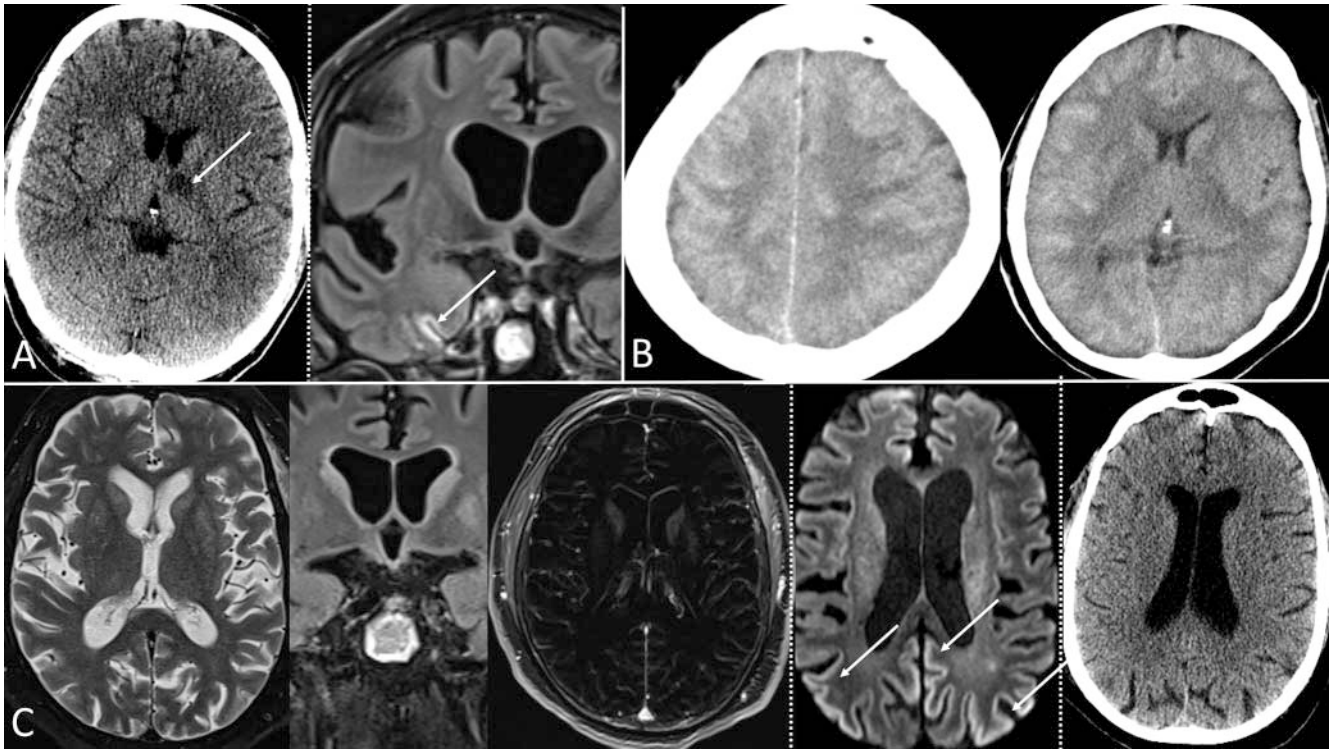
	No neuroimaging findings (n = 21)	**Neuroimaging findings present (n = 13)**	**Total (n = 34)**
Sex			
Female	23.8 % (n = 5)	23.1 % (n = 3)	24.2 % (n = 8)
Male	76.2 % (n = 16)	76.9 % (n = 10)	75.8 % (n = 26)
Age (median)	69 years	59 years	67.5 years (min. 7 months, max. 82 years)
Time to intubation (median)	5.5 days	8 days	6.5 (min. 1 day, max. 29 days)
Hospital stay (median)	23.5 days	19.0 days	21.5 days
Time between onset of symptoms and confirmed SARS-CoV-2 infection	5 days	4 days	5 days
Time between onset of symptoms and brain imaging	19 days	29 days	22 days (min. 0, max. 43)
Comorbidities			
Cardiac	57.9 % (n = 11)	75.0 % (n = 9)	64.5 % (n = 20)
Respiratory	36.8 % (n = 7)	25.0 % (n = 3)	32.3 % (n = 10)
Hemato-oncological	10.5 % (n = 2)	8.3 % (n = 1)	9.7 % (n = 3)
Renal	15.8 % (n = 3)	41.7 % (n = 5)	25.8 % (n = 8)
Neurological	33.3 % (n = 6)	8.3 % (n = 1)	23.3 % (n = 7)
Psychological	21.1 % (n = 4)	8.3 % (n = 1)	16.1 % (n = 5)
Endocrine	26.3 % (n = 5)	50.0 % (n = 6)	35.5 % (n = 11)
Gastrointestinal	21.1 % (n = 4)	25.0 % (n = 3)	22.6 % (n = 7)
ICU treatment	75.0 % (n = 15)	100.0 % (n = 13)	84.4 % (n = 28)
Ventilation mode			
None	5.3 % (n = 1)	0 % (n = 0)	3.2 % (n = 1)
Supplementary oxygen	26.3 % (n = 5)	0 % (n = 0)	16.1 % (n = 5)
Noninvasive	5.3 % (n = 1)	0 % (n = 0)	3.2 % (n = 1)
Invasive	42.1 % (n = 8)	76.9 % (n = 10)	56.3 % (n = 18)
ECMO	21.1 % (n = 4)	23.1 % (n = 3)	22.6 % (n = 7)
Neurological symptoms	42.9 % (n = 9)	53.8 % (n = 7)	47.1 % (n = 16)
Focal deficit	4.8 % (n = 1)	7.7 % (n = 1)	5.9 % (n = 2)
Epileptic seizure	4.8 % (n = 1)	0.0 % (n = 0)	3.0 % (n = 1)
Reduced consciousness	28.6 % (n = 6)	53.8 % (n = 7)	38.2 % (n = 13)
Psychiatric symptoms	14.3 % (n = 3)	0.0 % (n = 0)	8.8 % (n = 3)

Multiple microbleeds were the most frequent abnormality. These are rare in the healthy population, yet their incidence increases with age (> 80 years) and the presence of comorbidities, such as cerebral amyloid angiopathy or chronic arterial hypertension [12]. However, microbleeds are also known to occur in critically ill patients being treated in intensive care units, especially in patients with ARDS receiving intensified respiratory therapy [13]. The characteristic neuroimaging pattern described in this setting includes multiple cerebral microbleeds, most severely affecting the corpus callosum [12]. In our cohort a microbleed pattern compatible with critical illness encephalopathy was seen in 4 patients. This pattern has also been described in other studies investigating neuroimaging features in COVID-19 patients [9]. Furthermore, patients also showed multiple microbleeds not accentuated in the corpus callosum but affecting the white matter, both superficial and deep. This constellation might be due to therapeutic anticoagulation, potentially combined with some critical illness or ARDS component [14]. In severe COVID-19 cases,



▶ **Fig. 1** Hemorrhagic manifestations. **A**: Hemorrhagic manifestations included multiple callosal microbleeds, typical of critical illness or ARDS-associated encephalopathy (55-year-old and 54-year-old males, MRI, SWI/T2*GRE axial). **B**: Multiple microbleeds in the superficial and deep hemispheric white matter (57-year-old male; MRI, SWI axial). **C**: Microbleeds of both patterns were seen to be associated with subtle convexity subarachnoid hemorrhage (61-year-old-male; unenhanced axial CT) or **D**: convexity superficial hemosiderosis that was found to be associated with the vascular boundary zones in some cases (MRI, T2*GRE/SWI axial). **E**: Frank macrohemorrhage was also observed with typical hematoma (35-year-old female patient; MRI, left: T2w axial, right: T1w axial) and **F**: with atypical hematomas (left: 51-year-old female patient, unenhanced axial CT; right: 59-year-old male patient; MRI, T2* axial). Abbreviations: SWI – susceptibility-weighted imaging, GRE – gradient recalled echo.

▶ **Abb. 1** Hämorrhagische Manifestationen. **A**: Zu den hämorrhagischen Manifestationen gehörten multiple kallosale Mikroblutungen, die typisch für eine critical illness- oder ARDS-assoziierte Enzephalopathie sind (55-jähriger und 54-jähriger Patient; MRT, SWI/T2*GRE axial). **B**: Multiple Mikroblutungen in der oberflächlichen und tiefen weißen Substanz (57-jähriger Patient; MRI, SWI*GRE axial). **C**: Mikroblutungen beider Muster assoziiert mit subtiler Subarachnoidalblutung der Konvexität (61-jähriger Patient; natives axiales CT) oder **D**: superfizielle Hämosiderose der Konvexität, die in einigen Fällen mit den vaskulären Grenzzonen assoziiert war (MRT, T2*GRE/SWI axial). **E**: Makrohämorrhagien wurden sowohl als typische Blutung (35-jährige Patientin; MRT, links: T2w axial, rechts: T1w axial) sowie **F**: als atypische Blutung beobachtet (links: 51-jährige Patientin; natives axiales CT; rechts: 59-jähriger Patient; MRT, T2* axial). SWI = suszeptibilitätsgewichtete Bildgebung; GRE = Gradientenechosequenz.



▶ **Fig. 2** Ischemic, edematous, and hypoxic manifestations: **A** Ischemic manifestations included both subcortical (21-year-old male; unenhanced axial CT) and cortical stroke (74-year-old male patient; MRI, T2 FLAIR coronal). **B** Generalized edema (50-year-old female patient; unenhanced axial CT). **C** Furthermore, findings compatible with posthypoxic changes were both seen on MRI (signal changes in the basal ganglia with contrast enhancement) or residual cortical restricted diffusivity (68-year-old male patient; from left to right: MRI T2w axial, T2 FLAIR coronal, T1 subtraction axial, DWI axial) or unenhanced axial CT (67-year-old male patient; reduced gray-white differentiation). Abbreviations: FLAIR – fluid attenuated inversion recovery, DWI – diffusion-weighted images.

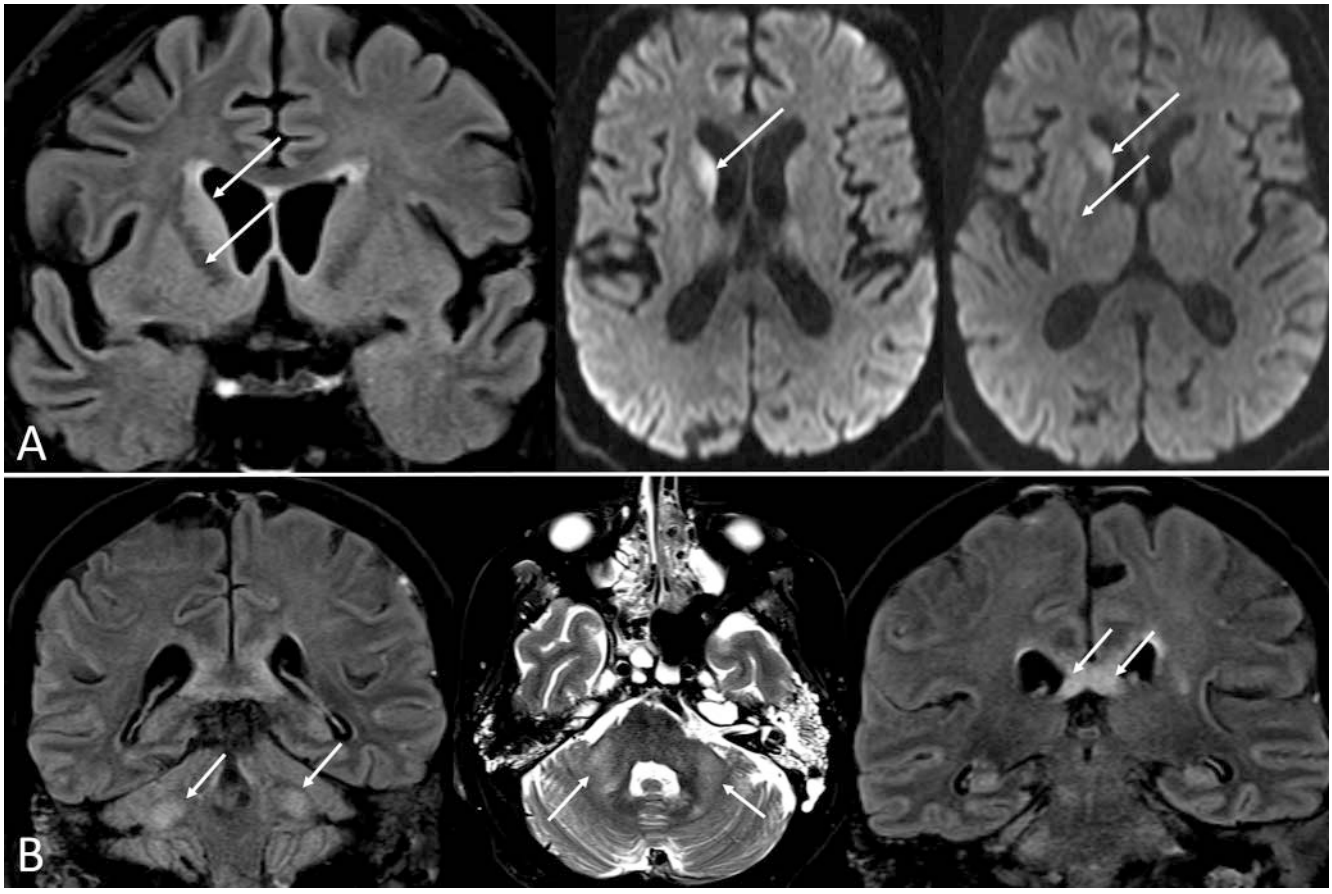
▶ **Abb. 2** Ischämische, ödematöse und hypoxische Manifestationen. **A** Ischämische Manifestationen umfassten sowohl subkortikale (21-jähriger Patient; natives axiales CT) als auch kortikale Schlaganfälle (74-jähriger Patient; MRT, T2-FLAIR koronar). **B** Generalisiertes Hirnödem (50-jährige Patientin; natives axiales CT). **C** Darüber hinaus wurden sowohl mit posthypoxischen Veränderungen vereinbarte Befunde im MRT (Signalveränderungen in den Basalganglien mit Kontrastmittelaffinität) als auch residuelle kortikale Diffusionsrestriktionen beobachtet (68-jähriger Patient; von links nach rechts: MRT T2w axial, T2-FLAIR koronar, T1 axial, DWI axial) oder natives axiales CT (67-jähriger Patient; verminderte Grau-Weiß-Differenzierung). ADC = apparenter Diffusionskoeffizient; FLAIR = fluid attenuated inversion recovery; DWI = diffusionsgewichtete Bildgebung.

the SARS-CoV-2 virus-induced derangement of the coagulation system as well as potential viral endothelial disturbances mediated by the ACE2-receptor might also be implicated in the pathogenesis of these microbleeds [15–17]. Other hemorrhagic manifestations included frank cerebral hematomas, focal cortical subarachnoid hemorrhage, and convexity hemosiderosis. Iatrogenic anticoagulation or blood pressure instability may also be potentially implicated in these events [18–20]. Of note, in some cases both sulcal subarachnoid hemorrhage as well as superficial siderosis were seen to be topographically related to the vascular boundary zones, potentially implicating impairment of cerebral autovasoregulation. Bleeding was also observed in the majority of patients in the retrospective study by Kremer et al. [11].

Two ischemic strokes were observed in our cohort. Preliminary studies show that the incidence of strokes may be elevated in hospitalized SARS-CoV2-infected patients, and that even young patients are affected [16, 21]. While these two strokes were not causally assigned, changes in the coagulation system with a resultant prothrombotic state, endothelial dysfunction, or cardiac affection with arrhythmia may be potential virus-associated causes of stroke recently described in the literature [22, 23].

Signs of hypoxic brain injury were also found in several patients while only one had a history of resuscitation. Episodes of inadequate oxygenation in COVID-19-associated ARDS despite respiratory therapy appears to be the most likely cause [24]. While 3 patients clinically showed symptoms of parainfectious and/or metabolic encephalopathy, there was no case of encephalitis or meningitis in our cohort as described in recent studies in patients with COVID-19 [9–11].

We observed several imaging findings that we cannot assign with certainty, such as one patient with T2 signal elevation of the middle cerebellar peduncles and the fornices, most likely representing mild vasogenic edema, as well as one patient with primarily cytotoxic edema confined to the striatum unilaterally. As both patients had multiple comorbidities in addition to severe COVID-19, including liver and renal failure, a broad range of differentials, including metabolic and toxic besides direct viral affection, has to be taken into account.



▶ **Fig. 3** Miscellaneous manifestations. **A** A 63-year-old-male patient showed unilateral signal changes in the striatum with subtle T2 hyperintensity and restricted diffusivity. ADC was clearly reduced (down to 426 × 10–6mm2/s) and follow-up CT scans 9 days later did not demarcate ischemic changes, not shown (from left to right: T2 FLAIR coronal, DWI axial, DWI axial). LP was unremarkable. **B** A 54-year-old male patient showed bilateral signal changes in the middle cerebellar peduncles and the fornices consistent with mild vasogenic edema (no restricted diffusivity, not shown). Differentials discussed in both cases included metabolic/ toxic as well as direct viral causes (from left to right: T2 FLAIR coronal, T2w fs axial, T2 FLAIR coronal). Abbreviations: ADC – apparent diffusion coefficient, FLAIR- fluid attenuated inversion recovery, DWI – diffusion-weighted images.

▶ **Abb. 3** Sonstige Manifestationen. **A** 63 Jahre alter Patient mit unilateralen Signalalterationen des Striatums mit subtiler T2-Hyperintensität und eingeschränkter Diffusion. Der ADC war deutlich reduziert (bis 426 × 10–6mm2/s), in der Verlaufs-CT 9 Tage später zeigten sich keine ischämischen Demarkierungen (nicht gezeigt) (von links nach rechts: T2-FLAIR koronar, DWI axial, DWI axial). Die Lumbalpunktion war unauffällig. **B** 54-jähriger Patient mit bilateralen Signalveränderungen in den mittleren Kleinhirnstielen und den Fornices, die einem subtilen vasogenen Ödem entsprachen (keine Diffusionsrestriktion, nicht gezeigt). In beiden diskutierten Fällen kommen sowohl metabolische/toxische als auch direkte virale Ursachen differenzialdiagnostisch in Betracht (von links nach rechts: T2-FLAIR koronar, T2w fs axial, T2-FLAIR koronar). ADC = apparenter Diffusionskoeffizient; FLAIR = fluid attenuated inversion recovery; DWI = diffusionsgewichtete Bildgebung.

This study is limited by its sample size as well as its retrospective and observational study design. Moreover, it has a case selection bias as in particular, younger patients with severe courses were transferred to our center from other hospitals for intensified critical care. The follow-up time is also limited (median 12 days from imaging acquisition until data acquisition). At the time of data acquisition most patients were still hospitalized. The clinical data, e. g., the patients' neurological symptoms, was only recorded from electronically stored patient data. Therefore, patients with mild neurologic manifestations might not have been captured. Moreover, most patients were invasively ventilated and for this reason sedated. Neurological assessment is very limited in these cases and cerebrospinal fluid analyses were only infrequently (n = 5) performed. Yet, we are not aware of a larger neuroimaging series in COVID-19 patients.

Key Points

Based on the analysis of this large cohort of SARS-CoV-2-positive patients, pathological neuroimaging findings seem to be relatively rare in general but do occur in a substantial proportion of patients with severe COVID-19 disease needing intubation or ECMO.

The majority of neuroimaging findings are probably critical illness- and therapy-associated although direct and indirect viral effects cannot be excluded. Thus, critically ill patients should be neurologically evaluated, and neuroimaging should be performed with a low threshold.

Further studies are necessary to determine prognostic aspects especially neurological and neuropsychiatric impact.

Conflict of Interest

The authors declare that they have no conflict of interest.

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