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BRAIN AND BLOOD VESSEL IMAGING FOR ISCHEMIC STROKE IN PATIENTS WITH COVID-19—DATA FROM THE LITERATURE AND CLINICAL CASES

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ABSTRACT

This study explores the relationship between patients diagnosed with ischemic stroke and SARS-CoV-2 infection. The focus is on the role of neuroimaging in confirming the diagnosis of ischemic stroke and guiding patient care. The COVID-19 pandemic has posed challenges in di-agnosing and treating patients with neurological pathologies due to the time-sensitive nature of stroke management. The objective of this study was to analyze cases of patients with ischemic stroke and SARS-CoV-2 infection, emphasizing the importance of neuroimaging in confirming the diagnosis. The study aimed to provide insights into the characteristics and clinical manifestations of these patients, contributing to our understanding of the neurological impacts of COVID-19. A retrospective analysis of hospitalized patients with a diagnosis of ischemic stroke and SARS-CoV-2 infection was conducted. The study focused on five representative cases, including patient de-mographics, medical histories, clinical symptoms, and imaging findings. Brain CT and MRI scans were performed to confirm the diagnosis of ischemic stroke. Among the 120 cases analyzed, 5 representative cases are presented. These cases include patients of varying age and gender with concurrent neurological pathologies and COVID-19 infections. Neuroimaging, such as CT and MRI, confirmed the diagnosis of ischemic stroke in these patients. Patients with SARS-CoV-2 in-fection and ischemic stroke often present with moderate to severe strokes, frequently involving large vessel obstructions. Neuroimaging plays a critical role in diagnosing and characterizing ischemic stroke in these patients. Identifying thrombotic angiopathy, vascular injury, and im-paired vascular autoregulation are essential for prompt diagnosis and treatment. This study emphasizes the significance of neuroimaging in managing patients with both COVID-19 and neurological pathologies, contributing to our understanding of the neurological implications of COVID-19.

Keywords: brain; ischemic stroke; computed tomography; magnetic resonance imaging; patients; COVID-19.

Introduction

Numerous pathways have been hypothesized for ischemic stroke in the context of COVID-19 infections, such as the association between severe COVID-19 illness and its more frequent appearance in elderly patients who are more likely to have many comorbidities that increase the risk of stroke. COVID-19-positive individuals appearing with large vessel obstructions showed a lower prevalence of pre-existing cardiac diseases and were younger than COVID-19-negative patients.

Strokes in patients with COVID-19 may have unique disease pathogeneses, patient demographics, clinical and neuroradiological features, with consequences for diagnosis and management. This study discusses the pathogeneses, clinical characteristics, and major neuroradiological features of strokes in COVID-19 patients.

It is essential to comprehend the demographic and clinical characteristics of stroke, because it represents an emergency. This study serves as a comprehensive survey of the literature, with the presentation of cases to highlight the features of ischemic stroke linked with COVID-19, and to explain its clinical significance.

Ischemic Stroke

The term "stroke" was first mentioned in 1599 as a lay term, and was described as the spontaneous onset of symptoms of a "stroke of God's hand", without being accepted into the medical lexicon at the time. Doctors used the name "apoplexy", which has been a diagnosis since the writings of Hippocrates (1).

Stroke is now described by the World Health Organization as a clinical syndrome characterized by the sudden onset of clinical signs of focal or global disturbances of brain function that may last for more than 24 hours or lead to death. It is divided into three types: ischemic, hemorrhagic, and subarachnoid hemorrhage. It is the second-leading cause of death and the third-leading cause of disability worldwide; of all strokes globally, 68% are ischemic and 32% are hemorrhagic strokes (2).

Acute ischemic stroke is the most common type of stroke encountered, accounting for many cases. The most common etiologies of ischemic stroke are atrial fibrillation or thromboembolism associated with atherosclerosis of the great arteries. For example, 11-29% of ischemic strokes are represented by occlusions of the vertebrobasilar arteries, occlusions of the internal carotid artery, or the M1 or M2 segment of the middle cerebral artery (3).

Over time, various types of interventions and diagnostic approaches have been analyzed and developed to achieve the best possible results in stroke, in order to reduce the number of deaths in stroke patients. Modern medicine has advanced rapidly and has helped doctors to clinically focus on endovascular stroke therapy and the use of thrombolytic agents in addition to classical treatments, in order to achieve the most favorable clinical responses (4).

Basically, when the blood vessels of the brain are blocked or even ruptured, this is often accompanied by displaced hemolysis, thrombus formation, stenosis in the cerebral arteries, and hemorrhage in the brain parenchyma, all of which lead to reduced oxygen and blood flow to the brain and, hence, the occurrence of stroke. Associated risk factors include modifiable factors such as high blood pressure, diabetes, obesity, tobacco use, and alcohol consumption. It is a neurological pathology with a devastating impact on the patient's quality of life, as it has serious consequences such as paralysis, dizziness, and amnesia (5).

Imaging in ischemic stroke

Modern imaging comes to the aid of identifying stroke, with computed tomography (CT) or nuclear magnetic resonance (MRI). The most common form of diagnostic imaging is CT, as it is the most available technology in hospitals, and always has a 24-hour guard line; however, in hospitals that also have 24-hour MRI, then doctors prefer to use nuclear magnetic resonance because it visualizes better and more accurately than CT and, of course, excludes radiation exposure. For the radiologist, the information provided by neurologists or emergency doctors before starting the CT or MRI scan is important (6).

Thus, the radiologist must know the onset of symptoms, the clinical examination performed, in addition to the objective neurological examination, the National Institutes of Health Stroke Scale (NIHSS) score, and personal pathological history. Among the most important objectives of CT or MRI scanning, we can list identification of vessel status, exclusion of intracranial hemorrhage, determination of the extent of ischemic lesions, and early and accurate identification of the infarct core and ischemic plume (6).

CT imaging generally helps us to exclude hemorrhage, to distinguish ischemic from hemorrhagic stroke, but it can also identify early changes such as hyperdentate arterial signs, loss of grey matter interface, white matter and inflamed brain test, and darkening of the insulin chord or lentiform nucleus. Diffusion-weighted nuclear magnetic resonance is effective in identifying hyperacute ischemia, but it can also detect abnormal cytotoxic edema in the early stage, and can clearly differentiate between ischemic lesions and the rest of the unaffected brain (7).

Thrombosis in COVID-19

COVID-19 has been linked to higher rates of arterial and venous thromboses in the pulmonary circulation as well as systemic circulation. The incidence rate of arterial thrombosis varies between 2.8% and 3.0% (8). Multiple reasons for thrombosis have been hypothesized, but there is

growing consensus that it starts with the activation of innate immune cells in relation to the beginning of a viral infection. The interplay between the innate immune system and thrombosis is intricate (9). It involves interactions among intravascular tissue factor stimulation, innate immune cells, thrombocytes, endothelial cells, and the products of neutrophils, which may trigger the connection route of coagulation. This idea is fundamental to the principal theory driving the coagulopathy related to COVID-19.

Postmortem histopathological examinations of all organ systems found in patients infected with SARS-CoV-2 revealed macrovascular and microvascular thromboses in the arterioles, capillaries, and venules composed of platelets, fibrin, erythrocytes, and leukocytes, indicating that SARS-CoV-2 causes a disorder of the vascular system instead of simply contaminating the airway.

Stroke mechanisms in COVID-19

The main possible explanation consists of the growth of a cytokine storm and stimulation of the immune system, embolic incidents perpetuated by existing or novel arrhythmias, hypoxia-dependent ischemia correlated with grave pulmonary disease, thrombus formation in microangiopathy, pathology of the endothelium, and multifaceted initiation of coagulation. The research results, stating that stroke occurs in 5.7% of patients with life-threatening illness compared to 0.8% of patients with relatively mild COVID-19 disease, reinforces the theory that COVID-19 plays an important role to stroke risk, varying on the level of illness; patients with a greater severity of the disorder have a greater likelihood of developing a stroke (10, 11).

Increased D-dimer concentrations in COVID-19-infected individuals with acute ischemic stroke reflect stimulation of the coagulatory and innate immune systems, which appears to be a consistent factor throughout the already reported data (12, 13).

Over 90% of COVID-19-positive individuals with sudden large vessel obstruction in New York had increased D-dimers, and 42% had acute ischemic stroke clinical signs instead of the usual respiratory symptoms (13). In particular, individuals appeared with stroke signs days prior to manifesting COVID-19 manifestations, indicating that there may be an elevated risk of thrombosis from the earliest stages of the illness (14). A previous assessment revealed a consistent rise in D-dimer concentrations in individuals with severe COVID-19 illness comparing to those with mild disease (15).

A cytokine storm, leading to raised levels of both interleukin-6 and C-reactive protein, has been linked with an elevated risk of stroke and myocardial infarction in healthy persons, and should also be considered.

The main reason of mortality recorded is respiratory failure, owing to the emergence of acute respiratory distress syndrome. Several studies have shown an elevation in arterial and venous thromboses, which contributes to the seriousness of the condition. This observation has included an increase in the frequency of strokes among younger individuals or individuals without previous stroke risk factors (16-20). Numerous risk factors connected with SARS-CoV-2 may cause a greater severity and earlier onset of acute ischemic stroke, such as generalized hypercoagulability; aberrantly immune reactions resulting in cytokine-release syndrome; destruction of endothelial cells resulting in a greater inflammatory response and thrombus formation; chemical imbalances of the renin–angiotensin–aldosterone system; and direct cytotoxic impacts on the nervous system (16-20). This study offers a summary of SARS-CoV-2 and the processes behind the formation of thromboses, which contribute to acute ischemic stroke in SARS-CoV-2 patients.

Even though the mechanism of ischemic stroke that is linked with COVID-19 is unknown, it has been suggested that inflammatory cytokine storms may promote hypercoagulable states or endothelial dysfunction (21). Numerous studies have also highlighted the various methods through which SARS-CoV-2 may induce neurologic problems including stroke. Many of these processes center on angiotensin-converting enzyme-2 (ACE-2), the binding site of SARS-CoV-2, and its role as a trigger for a cascade of events that result in vasoconstriction, hypertension, or thrombus instability. Additional studies indicate that immune-mediated processes, including the overexpression of cytokines, hypercoagulable conditions, and

thromboembolisms, may be possible causes of stroke (22-24). COVID-19 has been discovered to be strongly linked with ischemic stroke, due to the presence of possible stroke-causing variables.

In COVID-19 instances, a wide range of vascular inflammation-related consequences, especially AIS, have been recorded, with a variety of hypothesized molecular explanations (25-27). SARS-CoV-2 enters host cells through attaching to angiotensin-converting enzyme 2 (ACE-2) receptors that are present in many places, particularly the vascular endothelium, as well as neuronal, pulmonary, and cardiac tissue. Laboratory investigations of coronavirus-infected transgenic mice expressing human ACE-2 receptors have uncovered a multiorgan system lymphocytic inflammatory reaction characterized by vasculitis of the central nervous system (28, 29). Postmortem discoveries of viral aggregates inside vascular endothelial cells and deposits of inflammatory cells have resulted in the conclusion that direct viral-induced endothelial inflammation is an additional cause of organ failure and hypercoagulability in COVID-19 patients (30, 31).

COVID-19 could enhance the risk of stroke by a dual mechanism involving the expression and viral uptake of ACE-2 receptors. Initially, direct contamination of the brain endothelium, which contains the ACE-2 receptor, may increase the risk of virally induced vasculitis. Furthermore, blockage or depletion of ACE-2 receptors by viral infection and endocytosis upon cell entrance may reduce ACE-2 activity, hence reducing angiotensin production and compromising cerebral vascular autoregulation. Lastly, the hypoxia caused by a severe COVID-19 lung infection may further raise the risk of stroke by reducing the oxygen supply.

Materials and Methods

This study provides an overview of a group of inpatients with vascular pathologies and COVID-19, and highlights the importance of using imaging to quickly and correctly diagnose ischemic stroke, which also helps us to correctly approach the treatment and care of patients even in the context of a pandemic. Moreover, it emphasizes how imaging brings added confirmation when we have the objective neurological examination of the patient and the clinical diagnosis, to establish the final diagnosis and drive therapeutic decisions.

The analysis of the cases of patients diagnosed concomitantly with ischemic stroke and SARS-CoV-2 infection admitted to the neurology department of the Emergency Clinical County Hospital "St. Andrew" Constanta was carried out over a period of approximately 1 year and 9 months, between 1 January 2021 and 11 October 2022. The number of patients was 120, of which 62 were women and 58 were men. Ethics approval and consent to participate was provided by the Ethics Committee for Clinical Studies at the Constanta County Emergency Clinical Hospital (registration number 24/9.12.2022), which was conducted in accordance with the Declaration of Helsinki. Patient consent for publication was obtained; all subjects provided written informed permission before their enrolment.

Results

Distribution of ischemic stroke and number of deaths by sex

The number of patients diagnosed with ischemic stroke (acute, subacute, acute/subacute, transformed hemorrhagic) and deceased by sex can be found in Table 1. The age range of the patients is 53 years, with minimum 30 years and maximum 71 years.

Case presentations and imaging

Case 1

The first case was represented by an 82-year-old female, known in her personal pathological history with stroke sequelae, atrial fibrillation, hypertension, dyslipidemia, and chronic painful ischemic heart disease presented to the hospital's emergency care unit for language disorder and psychomotor agitation. These symptoms started 2 days before presentation to the hospital, and were accompanied by headache, dizziness, and vomiting that appeared the day before the presentation. On objective neurological examination, the patient was conscious, with slight psychomotor agitation, mixed aphasia, normal oculomotricity, no nystagmus, no motor

deficit, no superficial tactile sensitivity disorders, no coordination disorders, and cutaneous plantar reflex in bilateral flexion.

On presentation to the emergency department, a non-enhanced brain computed tomography (CT) scan revealed an appearance suggestive of supratentorial sequelae and a left parietal meningioma (Figure 1a, Figure 1b).

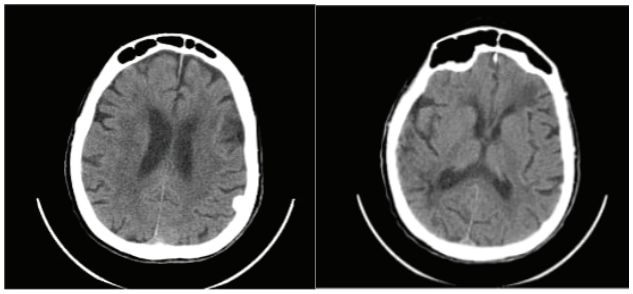

Figure 1. (a), (b): A native brain computed tomography (CT) scan suggests an appearance suggestive of supratentorial sequelae and a left parietal meningioma.

On day 5 of hospitalization, the patient underwent native cranio-encephalic and contrast-enhanced nuclear magnetic resonance imaging (MRI), and the MRI appearance was suggestive of a subacute stroke in the left middle cerebral artery territory (Figure 2).

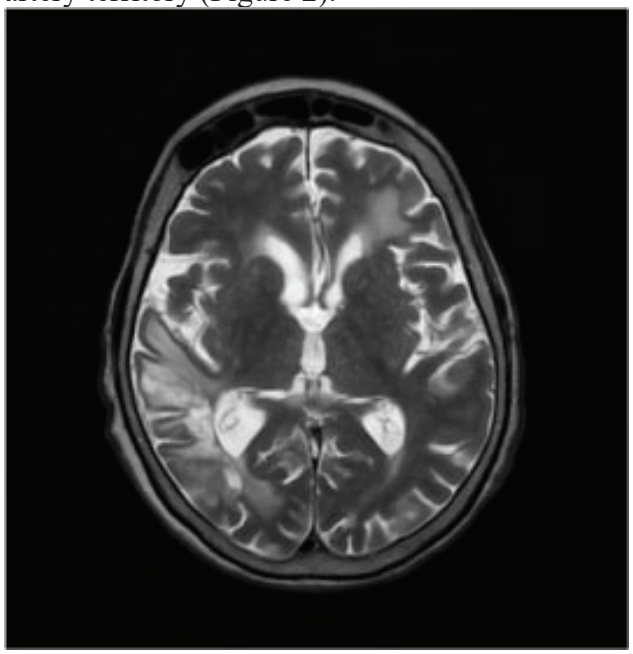

Figure 2. Cranio-encephalic MRI—moderate/high T2 lesion in the left middle cerebral artery territory; high T2 signal lesion with gliosis in the right parietal region.

On the 6th day of hospitalization, the patient underwent native CT examination of the chest and angio CT sequence for pulmonary arteries, due to a suspicion of pulmonary thromboembolism. An examination confirmed the diagnosis, and revealed moderate bilateral pleurisy, interstitial pulmonary edema, and pulmonary condensation processes. Thrombi in the left atrial auricle were also noted.

On the 7th day of hospitalization, the patient showed a positive RT-PCR (reverse transcription polymerase chain reaction) result for SARS-CoV-2. Given the positive test result for SARS-CoV-2, the imaging doctor was contacted to determine the severity score; the doctor stated that the lung lesions were classified as CORADS 3 (COVID-19 Reporting and Data System).

Following the laboratory tests performed during hospitalization, the patient showed the following changes: increased transaminases, mild leukocytosis with neutrophilia, hyperglycemia, slightly increased troponin T, increased urea, and increased inflammation problems.

After 7 days in the neurology ward, the patient was transferred to a COVID-19 support hospital for specialist treatment with the diagnosis of subacute stroke in the left middle cerebral artery territory and COVID-19 infection.

Case 2

A 63-year-old female patient, with no known pathological history, was admitted to the neurology department for language disorder, facial asymmetry, and motor deficit in the left limbs. At the time of admission, on objective neurological examination, the patient was conscious, cooperative, partially temporo-spatially oriented, with head and eyeballs deviated to the right, left central facial appearance, dysarthric, with left hemiplegia, and showing a plantar cutaneous reflex during left extension. At the time of admission, the patient underwent a rapid COVID-19 test, which was negative; however, when tested for SARS-CoV-2 RNA (ribonucleic acid) via RT-PCR, the patient showed a positive result. Moreover, at the time of admission, the patient underwent a brain CT scan which revealed an acute ischemic stroke of the right middle cerebral artery (Figure 3). The patient was transferred to a hospital that supports COVID-19, with a diagnosis of acute right middle cerebral artery ischemic stroke and

confirmed SARS-CoV-2 infection.

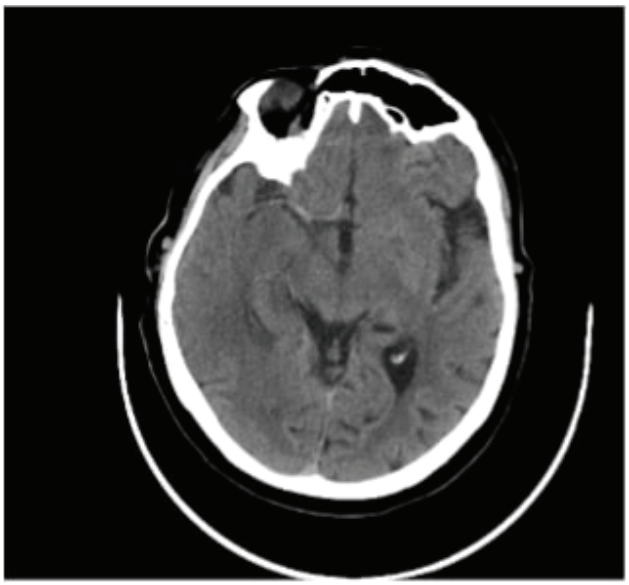

Figure 3. The brain CT shows a hyperdense right middle cerebral artery in the setting of an acute ischemic stroke.

Case 3

On October 2021, a 44-year-old male patient known to have hemorrhoids with active bleeding and melenic stools, without background treatment, was brought to the hospital's emergency care unit for paresthesia and a motor deficit in the upper and lower left limbs. At the time of the objective neurological examination, he was conscious, cooperative, temporo-spatially oriented, with left facial paresis, and left hemiparesis: upper limb 0/5, lower limb 4/5, left hemi-hypoesthesia, and left Babinski. On presentation to the hospital, the patient presented with a negative SARS-CoV-2 rapid antigen test and a negative SARS-CoV-2 RT-PCR test. A native brain CT performed at the time of presentation showed acute ischemic stroke in the superficial territory of the right middle cerebral artery (Figure 4).

On the 5th day of hospitalization, the patient showed a positive RT-PCR result for SARS-CoV-2, which is why he was transferred to hospital for COVID-19 support. During hospitalization, after paraclinical investigations, the patient presented severe microcytic hypochromic anemia, mild thrombocytosis, mild leukocytosis, biological inflammatory syndrome, elevated D-dimer levels, low ferritin, low serum iron, and slightly elevated total iron binding capacity.

The patient was transferred, with the diagnosis of acute ischemic stroke in the right middle cerebral artery territory and COVID-19 infection.

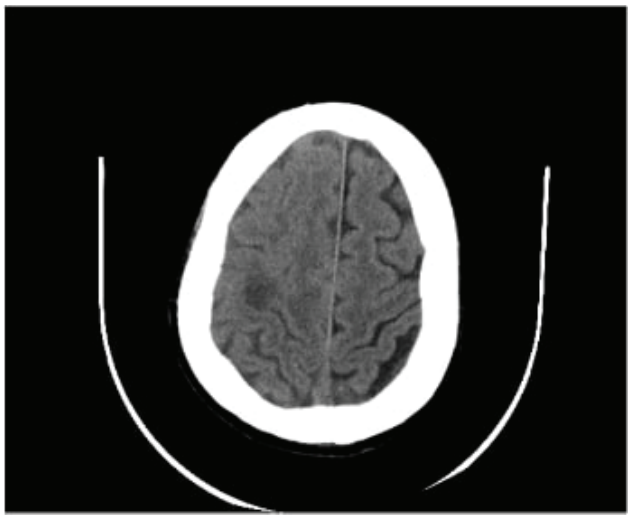

Figure 4. Non-enhanced CT shows a small hypodense lesion in the right frontal lobe.

Case 4

A 34-year-old male patient, known to have a trochanteric fracture of the left femur operated on in December 2021 and a fracture of the left sacral wing, was presented to the hospital for speech disorder and motor deficits in the right upper and lower limbs. At the time of presentation for objective neurological examination, the patient was conscious, with predominantly expressive mixed aphasia, no nystagmus, right central facial paresis, right 4/5 equally distributed hemiparesis, right hypoesthesia, and right Babinski. A native brain CT showed acute ischemic stroke in the left middle cerebral artery territory (Figure 5).

Furthermore, the RT-PCR test for SARS-CoV-2 was positive, so the patient was transferred to a COVID-19-supporting hospital. In terms of laboratory tests performed, the patient showed slightly elevated D-dimers and a biological inflammatory syndrome.

The patient was transferred, with the diagnosis of an acute stroke in the left middle cerebral artery territory and a SARS-CoV-2 infection.

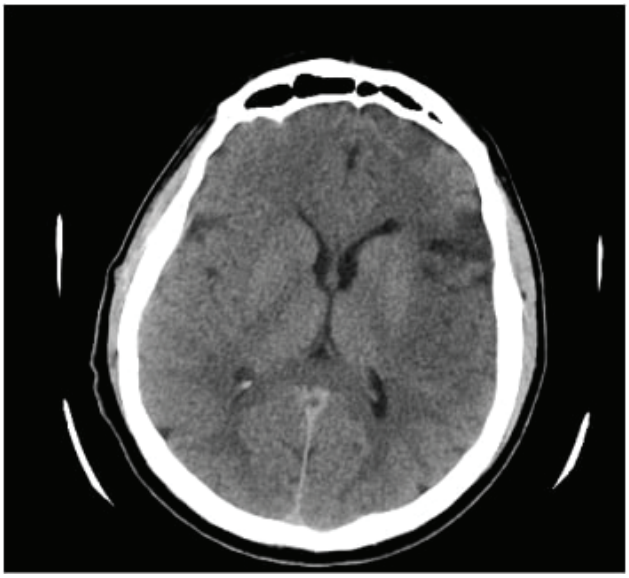

Figure 5. Brain CT shows a moderately hypoattenuating lesion in the left frontal, insular, and parietal lobes, and an acute ischemic stroke in the middle cerebral artery territory.

Case 5

A 65-year-old female patient, with known hypertension, chronic obstructive pulmonary disease GOLD stage IV, respiratory failure, NYHA class II/III heart failure, ischemic coronary artery disease, exertional angina pectoris, and type II diabetes mellitus that had been therapeutically neglected, presented with the sudden onset of slurred speech, an altered general condition, and a right limb plegic motor deficit.

At the time of presentation to the hospital's emergency department, the patient had a CT scan of the native brain that showed a normal appearance (Figure 6).

She also had a native chest CT scan with contrast material showing condensation processes in the medial lobe medial and lingula segments of the left upper lobe with atelectatic substrate; bilateral lung fibrotic changes; and mild interstitial edema and mediastinal adenopathy. When tested, the RT-PCR SARS-CoV-2 showed a positive result, which was why the infectious disease doctor recommended specialist treatment. On day 8 of admission, the patient underwent a native chest CT and pulmonary artery angio-CT sequence, with suggestive appearance of the following: pulmonary thromboembolism right inferior lobar artery; alveolar and interstitial infiltrates with tendency to confluence and consolidation, compatible imagistically with a COVID-19 viral pneumonia, CORADS 5, severity score 5points/25points; pulmonary condensation processes with most likely atelectatic substrate; bilateral pulmonary fibrotic changes; and mediastinal adenopathy.

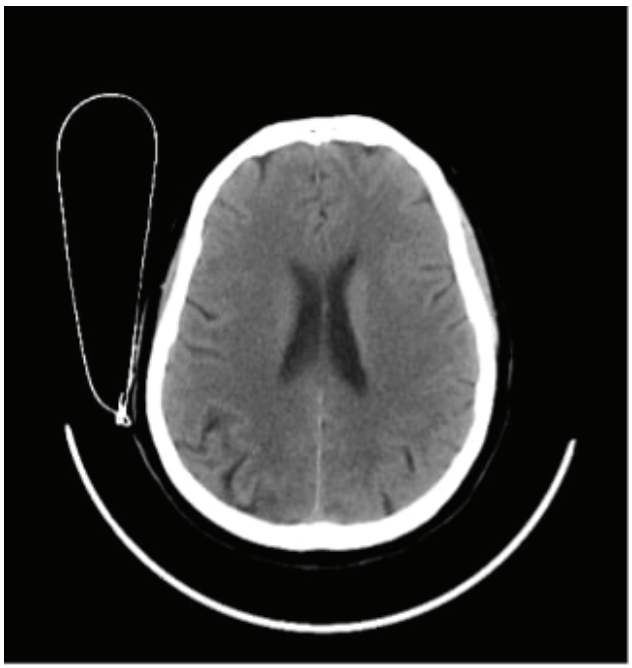

Figure 6. The brain scan of the patient, with no lesions detectable on CT.

On day 9 of admission, a native brain CT was performed, suggesting an appearance within the limits of age, unchanged from the previous examination. At 9 days, the patient also performed a SARS-CoV-2 RT-PCR test, which was negative.

On the 12th day of hospitalization, she underwent native brain MRI, which showed the following: late subacute microinfarction in the territory of the left anterior cerebral artery; a post-ischemic lacuna with hemorrhagic transformation in the territory of the left posterior inferior cerebellar artery; supratentorial demyelinating lesions with ischemic vascular substrate; bilateral mastoiditis; and bilateral sphenoidal sinusitis (Figure 7).

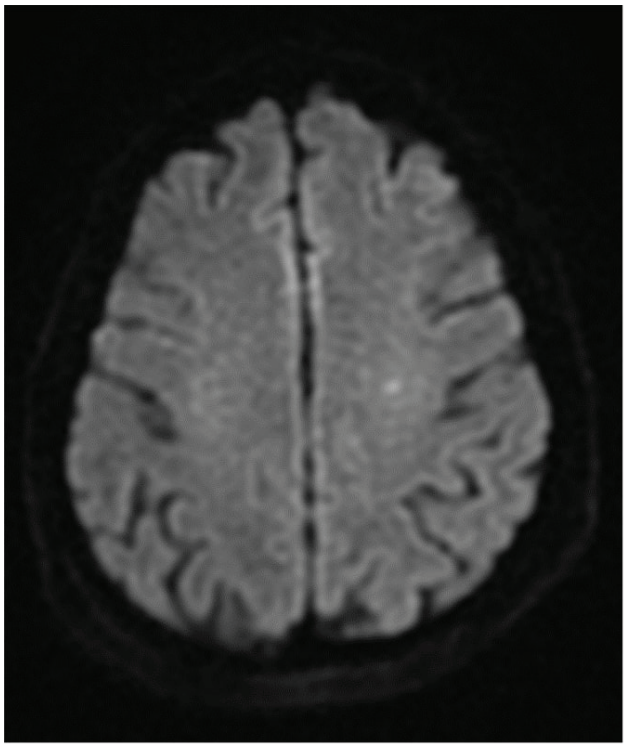

Figure 7. Non-enhanced brain MRI visualizing late subacute infarction in the territory of the left anterior cerebral artery—small foci with high DWI signal and moderate to low corresponding ADC map.

Under specialist treatment, the patient's clinical evolution was favorable, which was why she was discharged. At the objective neurological examination at discharge, the patient was conscious, cooperative, temporo-spatially oriented, with possible swallowing for solids and liquids, normal oculomotricity, no motor deficits, no sensitivity, or coronary disorders, bilateral symmetrical osteotendinous reflexes, bilateral plantar flexion cutaneous reflexes, with walking that was possible without support.

The patient was discharged with a diagnosis of subacute ischemic stroke in the left anterior cerebral artery territory and COVID-19 infection confirmed via RT-PCR testing.

Discussion

In our clinic, an analysis of the cases of hospitalized patients with a diagnosis of ischemic stroke and SARS-CoV-2 infection was performed, with a focus on imaging. Out of 120 cases, 5 cases were presented, of which 3 were female and 2 were male; the youngest patient was a 34-year-old male, and the oldest female was aged 82 years, admitted with concurrent neurological pathology and COVID-19 infection. Patients had a neurological diagnosis and SARS-CoV-2 infection from the onset of hospital presentation, or had neurological pathology initially, and then tested positive for COVID-19 during hospitalization. In these patients, the focus was on imaging, either brain CT or brain MRI, which confirmed the diagnosis of ischemic stroke.

In the United States, Yaghi et al. (32) conducted the first investigation on the incidence of ischemic stroke in COVID-19-infected individuals in New York, and discovered that 0.9% of all COVID-19-infected hospitalized patients suffered an ischemic stroke, with 63.6% of these deaths reported while hospitalized. Furthermore, in this study, a greater than usual proportion of the patients suffered a cryptogenic stroke. It was hypothesized that COVID-19-related cryptogenic stroke constituted a novel mechanism of stroke linked with an elevated risk of premature death (33). Additional preliminary investigations from New York, Italy, and Barcelona identified individuals with COVID-19 who had strokes and large vessel occlusions at a far younger age than would be typical (34-36). In addition, three investigations have shown that COVID-19 infection is a distinct risk factor for acute ischemic stroke and large vessel occlusion (37-39).

Patients with COVID-19 tend to have moderate to severe acute ischemic stroke with a higher incidence of large vessel obstruction. Significantly, imaging revealed that the majority of these acute ischemic strokes exhibited large vessel thromboses, emboli, stenoses, or several vascular territories distributions, with a considerably lower prevalence of small vessel strokes that diverged from typical acute ischemic stroke subtype patterns (40).

The associated neurological impairment was often significant (published median NIHSS scores varying from 19 to 21) (41-43). In addition, over forty percent of the patients were diagnosed with cryptogenic stroke, which often had an embolic radiologic aspect. In contrast, tiny vessel patterns were seldom recorded (44, 45).

Acute ischemic stroke represents the most prevalent neuroradiologic pathology observed

in COVID-19 patients with neurological symptoms, often affecting the major arteries (60–65% of instances) (46, 47). In a study, multiple vascular region ischemia was common, occurring in 26% of patients, but minor vessel blockage was observed in just 9% of patients (48). In another study, acute ischemic stroke in the vertebro-basilar area was prevalent, affecting 35% of individuals. Other publications have also verified the frequency of ischemic strokes in the posterior circulation. In one case, the vasculitic activity in an adult patient was widespread, affecting the bilateral ACA, MCA, vertebral arteries, and basilar artery (49). In research, the functional prognosis was negative in over 70% of individuals (50), and significant mortality was also seen in other groups (51, 52).

In two separate investigations (53, 54) conducted in Italy and the United States, the survival of COVID-19 and concomitant stroke patients was considerably worse compared to that of non-COVID stroke patients. The stroke patients accompanied by severe respiratory illness necessitating ICU hospitalization had a very high fatality rate (54). The occurrence of significant neurological signs (characterized as encephalopathy, stroke, or seizures) throughout the period of SARS-CoV-2 infection was demonstrated to be an important predictor of mortality in hospitalized individuals (55).

In summary, our collection of neurologic imaging data suggests that intrinsic thrombotic angiopathy, direct vascular injury, and impairment of the brain's vascular autoregulation can coincide with COVID-19 patients with neurological symptoms. The identification of these pathophysiologic processes and their neuroimaging counterparts is of the highest significance for a prompt diagnosis and treatment.

Based on the information provided, it appears that the cases analyzed in this study involved patients who presented with neurological pathologies and were diagnosed with ischemic stroke. These patients were found to have concomitant SARS-CoV-2 infection, either from the onset of hospital presentation or during the course of hospitalization. Therefore, it can be inferred that the focus of the study was on patients with neurological pathologies who were already diagnosed with ischemic stroke and subsequently tested positive for SARS-CoV-2 infection. The study does not specifically address patients without any prior neurological pathology who later developed ischemic stroke as a result of SARS-CoV-2 infection. This distinction is important when considering the generalizability of the findings to the broader population and understanding the specific impact of SARS-CoV-2 infection on the development and presentation of ischemic stroke. Further research is needed to investigate the relationship between COVID-19 and ischemic stroke in patients without any prior neurological pathology. The manuscript primarily focuses on neurological symptoms and ischemic stroke, which may explain the absence of detailed information on COVID-19 symptoms. It is essential for future research to collect comprehensive clinical data to better understand the link between COVID-19 and neurological conditions.

It is important to recognize that the prognosis of patients with ischemic stroke and SARS-CoV-2 infection can vary, depending on factors such as the severity of the stroke, the extent of neurological deficits, the presence of comorbidities, and the timely initiation of appropriate treatment.

The severity levels of COVID-19 in each case were not explicitly mentioned in the provided information. However, some relevant details were provided, such as lung lesions being classified as CORADS 3 in Case 1 and a suggestive appearance of COVID-19 viral pneumonia (CORADS 5, severity score 5/25) in Case 5. These indications suggest varying degrees of severity, with Case 5 potentially indicating a more severe presentation due to the presence of viral pneumonia.

Unfortunately, the provided information does not include the Ct values from the RT-PCR tests, which could provide further insight into the viral load and severity of the infection in each case. The provided information does not explicitly mention the long-term prognosis or outcomes of the five presented cases. The focus of the information is primarily on the clinical presentation, imaging findings, and the diagnosis of ischemic stroke in patients with concomitant SARS-CoV-2 infection.

The main viewpoint of the study is to

highlight the importance of neuroimaging in diagnosing ischemic stroke in patients with concomitant SARS-CoV-2 infection. The article emphasizes that neuroimaging, such as CT and MRI, play a crucial role in confirming the diagnosis of ischemic stroke, and guiding patient care and treatment decisions. By analyzing representative cases, this study provides insights into the characteristics and clinical manifestations of patients with ischemic stroke and SARS-CoV-2 infection. Overall, this research underscores the significance of neuroimaging in the context of the COVID-19 pandemic, contributing to the understanding of the neurological impacts of SARS-CoV-2 infection and emphasizing the role of imaging in managing patients with both COVID-19 and neurological pathologies.

Limitations

The analysis was based on a limited number of cases, which may not represent the full spectrum of patients with ischemic stroke and SARS-CoV-2 infection. A larger sample size would increase the generalizability of the findings. It may also be difficult to establish causal relationships or determine the temporal sequence of events. The study was conducted in a single neurology department, which may limit the diversity and generalizability of the findings to other healthcare settings or populations. The absence of a control group of ischemic stroke patients without SARS-CoV-2 infection makes it difficult to compare and assess the specific impact of COVID-19 on ischemic stroke presentation and outcomes. It is important to acknowledge these limitations, as they may influence the generalizability and robustness of the study's findings. Further research with larger sample sizes, prospective designs, and comprehensive clinical data is warranted to overcome these limitations and provide a more comprehensive understanding of the relationship between ischemic stroke and SARS-CoV-2 infection, but given that this topic is still under investigation, we believe that any small published information may help to create a final conclusion.

The provided information does not explicitly mention the presence or absence of characteristic symptoms associated with SARS-CoV-2 infection, such as fever, pneumonia, coughing, or other respiratory symptoms, for the analyzed cases. The focus of the information is primarily on the neurological symptoms and imaging findings related to ischemic stroke. However, it is stated that the patients were diagnosed with SARS-CoV-2 infection either from the onset of hospital presentation or during the course of hospitalization. This suggests that they likely exhibited symptoms or met the criteria for COVID-19 testing, but the specific details of their symptoms are not provided in the given text. It is important to note that the absence of information regarding characteristic COVID-19 symptoms in these cases does not imply that the patients did not experience them. Detailed clinical data, including symptomatology, would provide a more comprehensive understanding of the patients' overall presentation and aid in determining the relationship between COVID-19 symptoms and the development of ischemic stroke.

The manuscript provides a comprehensive overview of the clinical presentation and diagnosis of ischemic stroke in the context of SARS-CoV-2 infection. However, it does not delve into the long-term prognosis or outcomes, leaving important questions about the recovery and potential lasting effects of these patients unanswered. It would be valuable for future research to incorporate follow-up data to assess the short and long-term outcomes, which could offer insights into the impact of COVID-19 on stroke patients' recovery and overall health.

Conclusions

Defining the interactions between COVID-19 cases and the brain's vascular system is crucial for directing therapy for this complicated patient group. Ischemic stroke induced by COVID-19 has distinct clinical characteristics. Common risk variables are also observable, and their significance may have altered. Therefore, the risk of ischemic stroke should be considered when a patient with COVID-19 is hospitalized. The cases and findings from our study call into attention the existing stroke imaging techniques and the necessity for further imaging when COVID-19-positive individuals with stroke

symptoms report to the emergency unit. Patients could benefit from promptly beginning anti-inflammatory and anticoagulant medications. Nevertheless, more clinical studies must be conducted to provide proof.

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