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Imaging findings of two patients with isolated infarction of the splenium during COVID-19

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Abstract

Coronavirus disease 2019 (COVID-19) is caused by the virus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In the literature, this virus has been associated with coagulation dysfunction and arterial thromboembolism. In clinical practice, corpus callosum infarcts are very rare, and the incidence of isolated splenium infarct is very low. Here, two cases of isolated splenium infarct after COVID-19 are reported with clinical and imaging findings. These findings are thought to be useful in daily practice for our colleagues. In addition, differential diagnoses of this entity will also be discussed in this case report.

Keywords

COVID-19, corpus callosum, cerebral infarction, magnetic resonance imaging

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Introduction

The corpus callosum (CC) contains the largest commissural fibers, which connect the two cerebral hemispheres, and it is known to be the largest white matter tract in the brain. Rostrum, genu, body, and splenium are the components of the CC, which are anatomically aligned from the anterior to the posterior part of this organ, respectively. The abundant vascular supply of the CC renders this organ to be relatively protected from infarction.[1] Most CC is supplied by the pericallosal (a branch of the anterior cerebral artery), subcallosal, medial callosal arteries (branches of the anterior communicating artery), and the posterior pericallosal artery (a branch of the posterior cerebral artery) (Figure 1).[2] The pericallosal artery often provides the main blood perfusion for the body, whereas the subcallosal and medial callosal arteries supply the rostrum and genu of the CC.[3] However, splenium receives its blood supply mostly from the posterior pericallosal artery, which is a branch of the posterior cerebral artery, but the anterior pericallosal artery and accessory pericallosal arteries are the other blood supplies of the splenium.[4] Isolated splenium infarct is a rare entity and splenium infarcts are mostly associated with the infarction of the body of CC or adjacent cortical areas (Figure 2).[5]

Coronavirus disease 2019 (COVID-19) continues to be a significant threat to the global public health security. This virus is mainly transmitted from symptomatic patients by aerosol-like droplets that are produced during coughing or sneezing.[6] This virus does not only affect the respiratory system but also affects the heart, kidneys, eyes, gastrointestinal system, immune system, skin, endothelium, and the coagulation system.[7]

In this case report, two patients with positive laboratory results for COVID-19 who had visual symptoms are presented. The imaging results were consistent with isolated splenium infarcts.

Case reports

Case 1

A 19-year-old female patient was admitted to the emergency department. She had no history of trauma or medical surgery

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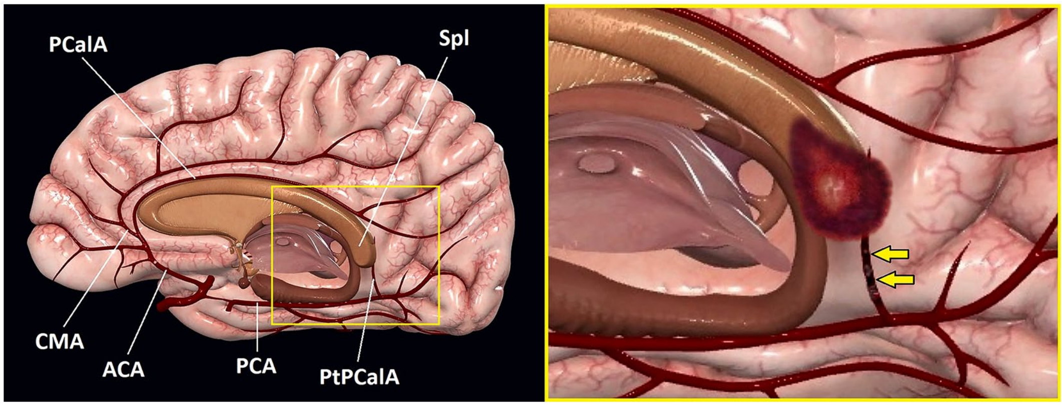

Figure 1. This three-dimensional illustration is a reminder of some important anatomical structures in the callosal–pericallosal area and important vessels around the corpus callosum. The magnified image demonstrates an isolated splenium infarct due to posterior pericallosal artery occlusion (yellow arrows). Figure 1 has been created by the Adobe Photoshop program (Adobe Inc., 2021. Adobe Photoshop, https://www.adobe.com/products/photoshop.html) based on the figures provided by the Complete Anatomy program (3D4 Medical, 2021. Complete Anatomy. Retrieved from https://3d4medical.com/).
Spl: splenium; PCalA: pericallosal artery; CMA: callosomarginal artery; ACA: anterior cerebral artery; PCA: posterior cerebral artery; PtPCalA: posterior pericallosal artery.

before her admittance to the hospital. She had complained of intermittent visual symptoms for 2 days, and no other symptoms were declared. She complained that she could hardly focus on details, especially when reading a book or watching television. The ocular movements were not affected, but the patient explained that objects seemed to be distorted for both eye evaluations. Her color vision was within normal limits in both eyes. Eye pupils were equally and bilaterally reactive to light. The fundoscopic examination was normal. The patient's general condition was evaluated as normal, conscious, and cooperative. Body temperature was 36.6°C, blood pressure was 107/62 mm Hg, and oxygen saturation was 97%. There was no power loss, and the Babinski test was negative in the physical examination. No tremor or dyskinesia was noted. The patient's total blood count, biochemistry, blood glucose level, and Brucella (Rose Bengal and immune capture with Coombs) tests indicated negative results. Anti-dsDNA antibodies, anti-Sjogren's Syndrome–related antigene A and B (anti-SSA and anti-SSB), antinuclear antibody (ANA), polymerase chain reaction (PCR) test for cytomegalovirus (CMV), and perinuclear and cytoplasmic antineutrophil cytoplasmic antibody (p-ANCA and c-ANCA) tests were all negative. However, the patient was found to be COVID-19 positive using the real-time polymerase chain reaction (RT-PCR) test. Before the patient received treatment at the clinic, the test was performed as part of a standard protocol. There were no cough, fever, chill, sore thought, or any other signs of viral infection.

The patient underwent magnetic resonance imaging (MRI) since it was believed that she had a migraine with aura. The magnetic resonance (MR) images revealed a lesion located in the splenium of the CC, which was slightly hypointense on T1-weighted and frankly hyperintense on T2-weighted images. Fluid-attenuated inversion recovery (FLAIR) sequence showed prominent hyperintense signals in the same location. The diffusion-weighted imaging (DWI) indicated a diffusion restriction in the splenium, consistent with acute infarction. MR angiographic images showed that there was a discontinuity in the terminal branches of the right posterior cerebral artery (Figure 2). Doppler ultrasound imaging showed no atherosclerosis, thrombus, occlusion, or stenosis in the carotid arterial system and vertebral arteries. The patient has been put on acetylsalicylic acid therapy, and there was improvement in her follow-up examinations.

Case 2

A 22-year-old female patient who had intermittent visual symptoms for 3 days was admitted to the emergency department. She complained that she was unable to see her surroundings clearly and the materials around her seemed to be deformed and blurred indicating a metamorphopsia. The ocular movements and her color vision were within normal limits in both eyes. Eye pupils were bilaterally reactive to light, and the fundoscopic examination was within normal limits in the ophthalmological evaluation. She had no history of trauma or any other chronic disease. She was generally in normal condition, oriented, and well-cooperated during the physical examination. Her body temperature was 36.9°C, her blood pressure was 110/59 mm Hg, and her oxygen saturation was 98%. Her neurological physical examination was normal, and no positive results were indicated with blood glucose level, total blood count, biochemistry, and Brucella

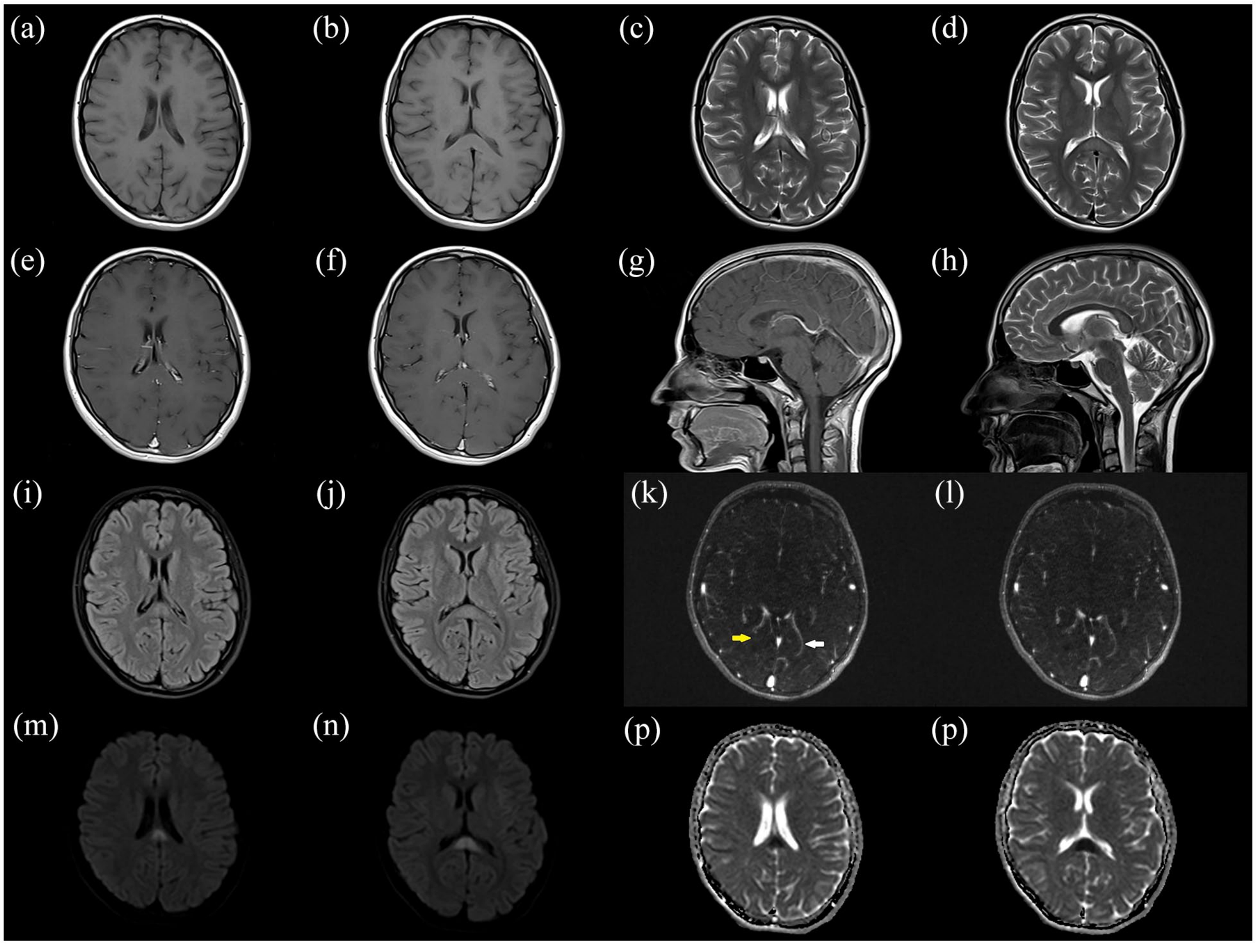

Figure 2. Magnetic resonance (MR) images of Case 1 (19-year-old female with isolated splenium infarct after COVID-19 infection). There is a slightly hypodense area in the location of splenium in T1-weighted images ((a) and (b)) and hyperintensity in the same location on axial T2-weighted images. There was no contrast medium enhancement in splenium on T1-weighted axial ((e) and (f)) and sagittal (g) series. T2-weighted sagittal image indicated the lesion in splenium with high signal intensity as well as axial FLAIR images ((i) and (j)). MR angiography shows the discontinuity of the right posterior cerebral artery on consecutive axial images ((k) and (l)). Diffusion-weighted images depict the diffusion restriction of splenium ((m) and (n)) with apparent diffusion coefficient maps ((o) and (p)).

agglutination tests. Anti-dsDNA, anti-SSA, anti-SSB, ANA, PCR test for CMV, p-ANCA, and c-ANCA tests were negative. Before the inpatient treatment at the clinic, an RT-PCR test indicated a positive result for COVID-19 infection. She was asymptomatic, and there was no sign of a viral infection like cough, fever, chill, sore thought, and so forth. The eye examination was normal, and an MRI was requested from the neurology department.

An MRI indicated a lesion in the splenium of CC, which was hyperintense on T2-weighted, FLAIR sequences, and hypointense on T1-weighted series. There was a marked diffusion restriction on diffusion-weighted MRI (Figure 3). The patient has been put on acetylsalicylic acid therapy; however, the follow-up process is unknown since the patient was never admitted to the hospital again for the follow-up examinations.

Discussion

Isolated CC infarcts tend to be rare and usually associated with infarcts on the other areas of cerebral hemispheres. Due to the small diameter of the perforating artery in the CC, blood from the neighboring branch arteries directly flows from the superior artery perpendicularly and the emboli tend to move to the middle cerebral artery. Therefore, the blood circulation of the CC is rarely blocked. In addition, due to the rich dual blood supply (from anterior and posterior circulation) even if the arterial blockage (due to stenosis or

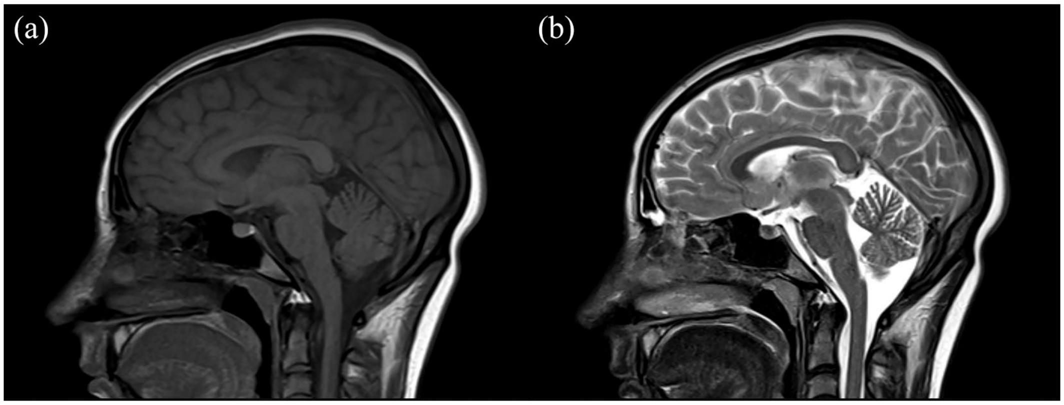

Figure 3. Magnetic resonance (MR) images of Case 2 (22-year-old female with isolated splenium infarct after COVID-19 infection). Sagittal T1-weighted image (a) shows no pathological signal in splenium; however, sagittal T2-weighted images indicate the focal hyperintensity of the splenium (b).

occlusion) occurs on one side, this blockage is compensated by the ramus anastomoticus. This renders CC infarcts a rarely encountered entity in clinical practice.[8] Splenium infarcts were found to be more than the other regions of the CC in the literature.[9] Atherosclerosis, hypertension, hyperlipidemia, diabetes, long-term smoking, and coronary heart disease are the main risk factors for developing CC infarction.[8] Both the cases in this report had no history or laboratory results indicating such risk factors for an infarction.

COVID-19 has been associated with an increased risk of venous and arterial thromboembolism due to coagulation dysfunction. This phenomenon was thought to occur due to immunothrombosis consequent to the recent infection rather than true thromboembolic events.[10] Hypercoagulable events have been reported in around 50% of cases with severe COVID-19.[11] Venous thromboembolism seems to be more frequently encountered as a thromboembolic complication of this disease, compared with arterial thrombosis.[12] To date, the real prevalence of thromboembolic complications of COVID-19 remains unknown, and much more investigations are needed to provide and gather patient data and analyze them with systematic and comprehensive methods.

Confusion, gait ataxia or truncal ataxia, delirium, dysarthria, increased muscle tone, new-onset seizure, hemispheric disconnection syndromes, astereognosis, pseudoneglect, and visual apraxia are the commonly expected clinical symptoms of splenial pathologies.[13] Negative Babinski test was mentioned in the patient records of Case 1, and this test is known as one of the upper neuron signs of acute ischemic stroke.[14] Besides, no meningeal signs were found in both patients during the routine neurological examinations. Visual symptoms are a predictable result of a splenic infarct because splenium provides communication of the somatosensory information between the two halves of the visual cortex at the occipital lobes via the fibers of forceps minor. Due to this anatomical fact, both cases in this report presented with visual symptoms. The visual information would be processed in the temporal, parietal, and occipital lobes across the cerebral hemispheres, and it is hypothesized that a disrupted transfer of visual information at the splenium and the major forceps leads to metamorphopsia in which the shape of objects appears distorted.[15] A study in the literature investigated 59 patients with CC infarcts, 7 of them were restricted to CC territory, and one of those patients with infarction limited to CC had vertigo and double vision in the research.[16] Another article in 2021 reported a case with homonymous hemianopsia and emphasized that there had been only 10 previous reports of isolated splenium infarcts in the literature. Within those cases, no case had been reported with homonymous hemianopsia before, while four of them had metamorphopsia.[17] In this current case report, metamorphopsia came to the forefront as a visual symptom.

Trauma may be another reason to be discussed in the etiology of such rare infarcts. Vasospasm has been proposed as the common mechanism to explain the etiology of post-traumatic cerebral infarcts, and the other possible mechanism is thought to be the sharing-associated vascular injuries.[5] When discussing the effect of trauma on the splenium, one of the most important differential diagnoses is diffuse axonal injury (DAI) to be mentioned. DAI lesions cause similar signal alterations in DWI as well as splenic infarcts.[18]

Lymphoma and multiple sclerosis are other differentials to be discussed. Both these diseases have specific clinical symptoms, physical examination findings, and laboratory examination results. However, lymphoma is known to cause restricted diffusion and has low apparent diffusion coefficient values, reflective of dense cellularity.[19] Lymphomas may have a similar appearance to splenium infarcts in conventional MR sequences (hypointense in T1-weighted, hyperintense on T2-weighted, and FLAIR images). Active white matter lesions of multiple sclerosis and lymphoma would enhance with contrast medium. In addition, further

MRI techniques like MR spectroscopy and MR perfusion studies are helpful in diagnostic challenges.

Toxic encephalopathies may be the cause of hyperintensities in splenium on T2-weighted imaging. Marchiafava–Bignami disease, which is attributed to vitamin B deficiency, may result in demyelination and necrosis of the CC. Metronidazole-induced encephalopathy may also be manifested as hyperintense lesions and may involve CC and splenium. In addition, epilepsy may cause transient lesions of the splenium, which may show diffusion restriction, hyperintensity on FLAIR and T2-weighted images and does not enhance on MR images.[20]

The total blood counts and peripheral blood smear tests showed no sign of hematologic anomalies. There were no specific clinical symptoms or physical examination findings for demyelinating diseases, and the patients had no history of trauma or toxic exposure. Brucella tests were also studied for both patients since it is still an endemic disease in the area.[21] One of the patients was admitted with double vision, but the physical examination revealed blurred vision in both eyes as in the other case. Blurred vision might also be explained by neurobrucellosis, even though it is a rare entity to explain this symptom.[22]

Sparr and Bieri mentioned about four cases in their brief report who had splenium infarct in the age of COVID-19. All the cases in this report had vascular risk factors and were older than 50 years, assumed to be exacerbated by hypoxia, renal failure, inflammation, and coagulopathy due to COVID-19. Two of them were isolated to the CC; one of them, splenial infarction, was almost certainly cardioembolic, and the other case was likely a variant of posterior reversible encephalopathy syndrome due to renal failure.[23] The cases in the current report were younger, with no known vascular risk factors, and the infarcts were isolated in the splenium.

For the reported cases in this article, a cerebral angiography would be more informative; however, there were no other radiological examinations other than those mentioned in this report in the hospital records. As shown in Figure 2, MR angiography indicated the discontinuity of the right posterior cerebral artery, which is very difficult to estimate to be occurred due to atherosclerosis or an embolism. DWI and FLAIR images showed the isolated lesion in the splenium for both cases. However, there is another entity to be mentioned called cytotoxic lesion of the corpus callosum (CLOCC) due to COVID-19, which may also be present with an isolated lesion indicated by DWI and FLAIR images.[24,25] Although there are not many reports in the literature, and the underlying mechanism is not fully understood, the swelling of the neurons in the CC is thought to be a result of the release of the cytokines triggered by COVID-19 in this disease. These triggering mechanisms were classified as drug therapy, infections, malignancies, subarachnoid hemorrhage, trauma, metabolic disorders, and other entities mentioned in the literature. High altitude sickness, hypertension in eclampsia or pre-eclampsia, seizures or status epilepticus, and numerous immune-related entities were included in the other entities group.[26] The cases presented in this article had no such etiologies in patients' histories or laboratory findings that were compatible to be a reason for CLOCC.

Conclusion

To summarize, there is not much available information about splenium infarcts due to COVID-19 in the literature, and the cases in this report might be assumed to be unique and rare in clinical practice. There might be other specific regions of the brain in which the tissue infarcts are unusual to occur due to COVID-19, which have not been reported yet. To understand the etiology and specifically affected regions of the brain by this viral infection, there should be more reports and studies in the literature. The dissemination of the knowledge and awareness of such unique behavior of this disease would be beneficial for all clinicians.

Author contributions

M.K. and V.K. contributed to the conception and design. M.K. and Ş.K. contributed to the acquisition of data. V.K. and Ş.K. contributed to the interpretation. V.K., M.K., and Ş.K. contributed to the literature review. M.K. contributed to the supervision. V.K. contributed to the manuscript drafting. M.K. contributed to the critical review.

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Ethical approval

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Informed consent

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