

Hemorrhagic leukoencephalitis due to SARS-CoV-2. Case report

Leucoencefalitis hemorrágica por SARS-CoV-2. Presentación de caso

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Summary

In recent years, the SARS-CoV-2 virus has been deeply studied in conjunction with its extrapulmonary manifestations and possible complications such as neurological manifestations. There are various pathophysiological situations regarding neurological compromise from the virus, among which vascular compromises such as ischemic manifestations, hemorrhages, and leukoencephalopathy have been described. This case presents a patient with findings of acute hemorrhagic leukoencephalitis, a post-infectious demyelinating disease in the context of a patient with SARS-CoV-2 virus infection.

Resumen

En los últimos años, el virus SARS-CoV-2 se ha estudiado profundamente en conjunto con sus manifestaciones extrapulmonares y las posibles complicaciones, como las manifestaciones neurológicas. Existen diversas hipótesis fisiopatológicas en cuanto al compromiso neurológico por el virus, entre estas se han descrito las afecciones vasculares como manifestaciones isquémicas, hemorragias y leucoencefalopatía. Este caso presenta una paciente con hallazgos de leucoencefalitis aguda hemorrágica, una enfermedad desmielinizante posinfecciosa en un paciente con infección por virus SARS-CoV-2.

Key words (MeSH)

SARS-CoV-2
Leukoencephalitis, acute hemorrhagic
Respiratory distress syndrome

Palabras clave (DeCS)

SARS-CoV-2
Leucoencefalitis hemorrágica aguda
Síndrome de dificultad respiratoria aguda

Case summary

A 39-year-old female patient from Haiti with no history of medical conditions was admitted by ambulance with acute altered consciousness. She was found drowsy by a family member, with no signs of trauma and emetic contents in her oral cavity. Upon admission, she was drowsy and unresponsive to stimuli. Suspected cerebral hemorrhage, a brain CT scan was performed, which showed nonspecific low densities in both globus pallidus, without acute bleeding or other abnormalities (Figure 1). The initial paraclinical study included a toxicology panel with no positive findings. Subsequently, she developed progressive neurological and respiratory deterioration, with consolidations on chest X-ray, leading to suspicion of pneumonia. RT-PCR confirmed SARS-CoV-2 infection and acute respiratory distress syndrome (ARDS), which required orotracheal intubation. In order to expand on the findings of the brain CT scan, a simple brain MRI with contrast medium was performed, which showed extensive and confluent high T2 signal in FLAIR sequences in the periventricular, deep, and subcortical white matter of both cerebral hemispheres, extending to all regions of the corpus callosum and corticospinal tracts (Figure 2). Additionally, small foci of high signal involving both globus pallidus and subtle high signal in the middle cerebellar peduncles and white matter of the cerebellar hemispheres were observed. Magnetic susceptibility sequences showed extensive microhemorrhages scattered throughout all the regions of white matter described above and in some regions of the brainstem (Figure 3). No areas of restriction were observed in the diffusion sequences, and after intravenous gadolinium injection, small foci of enhancement measuring approximately 7 mm were visualized in the globus pallidus (Figure 4).

Based on the findings, a diagnosis of acute hemorrhagic leukoencephalitis was considered. Treatment was initiated with systemic steroids and antimicrobials, with good clinical progress and improvement in symptoms, resolution of the altered state of consciousness, and mental functions.

Discussion

It has been widely documented that the SARS-CoV-2 virus -CoV-2 virus is an agent that can cause neurological pathology. Different pathophysiological mechanisms have been proposed to explain this phenomenon, including direct access of the virus to the central nervous system (CNS) via the olfactory pathway (neurotropism), which allows the virus's S protein to interact with angiotensin-converting enzyme 2 (ACE2) in the CNS, generating an uncontrolled inflammatory response.

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Figure 1. CT scan. Low ovoid density of the pale globules, with no other alterations.

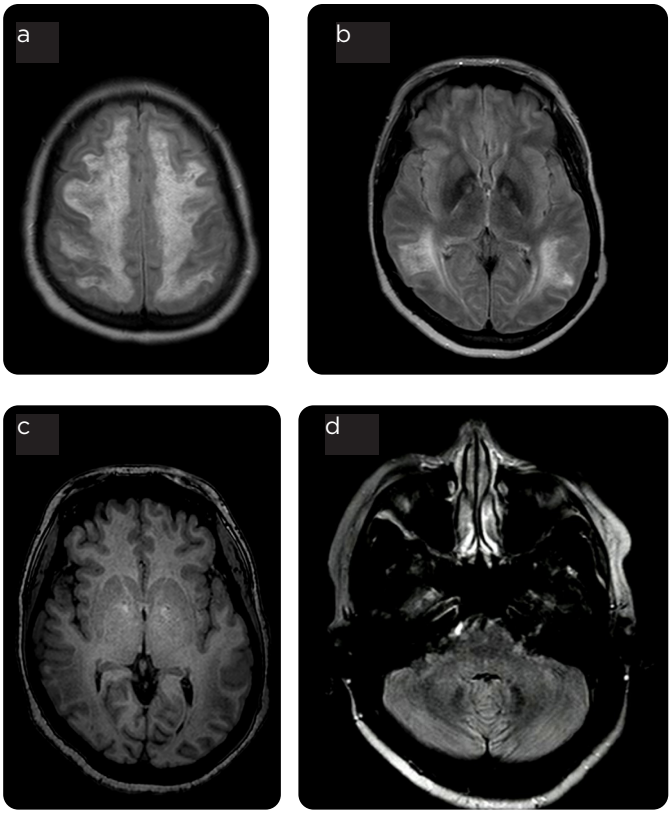


Figure 2. a and b) Axial FLAIR sequences enhanced in T2. Diffuse high signal in the subcortical, deep, and periventricular white matter of both cerebral hemispheres with diffuse punctiform foci of low signal. c) High signal in the globus pallidus, in T1-weighted sequences. d) Few poorly defined areas with high signal in FLAIR sequence with T2 information in the middle cerebellar peduncles and, to a lesser extent, in the pons.

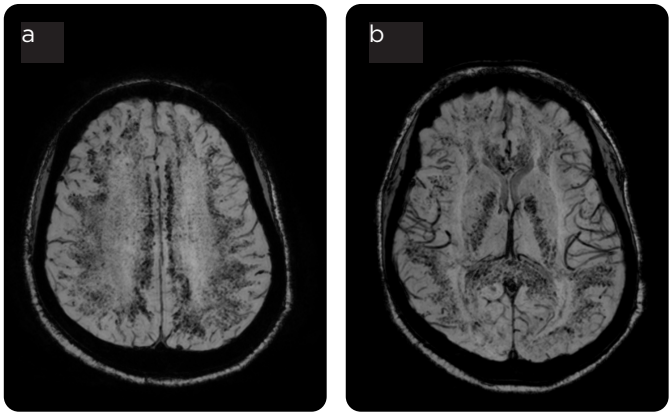


Figure 3. SWI MRI. Juxtacortical and subcortical microhemorrhages and, to a lesser extent, in the deep white matter, in the posterior arms of the internal capsules, in the corpus callosum, and in the globus pallidus.

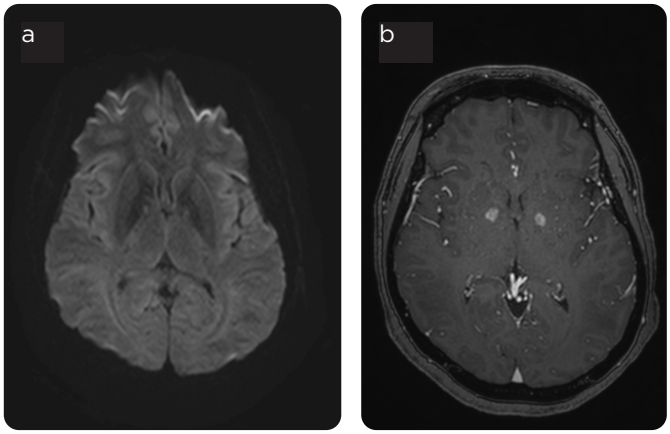


Figure 4. a) DWI MRI without areas of diffusion restriction. b) Post-gadolinium T1-weighted sequence: nodular enhancement in the medial region of both globus pallidus.

Another hypothesis suggests indirect damage to neural tissue due to an excessive systemic inflammatory response (1).

CNS involvement by the SARS-CoV-2 virus has been classified into five categories: 1) direct invasion of the CNS; 2) cytokine storm; 3) coagulopathy; 4) post-infectious effects due to a delayed immune response; and 5) side effects resulting from hospitalization or prolonged illness (2).

The most common neurological manifestations described in the literature are nonspecific and include headache, seizures, altered consciousness, and disturbances of the sense of smell or taste, with the latter being the most frequent (3). In a 2020 study of 185 patients, the most frequent findings in the CNS were those associated with microvascular disease (59% of cases), followed in order of frequency by ischemic manifestations, macrohemorrhages, leukoencephalopathy, and olfactory bulb lesions with alterations in their MRI signal (4).

The case documented here describes a patient with findings consistent with acute hemorrhagic leukoencephalitis, a hyperacute monophasic demyelinating disease that is part of the spectrum of acute disseminated encephalomyelitis (ADEM). This is a form of post-infectious demyelination, in which a previous viral or bacterial infection

has been demonstrated in up to 75% of cases (5). Viral infections, including those caused by coronaviruses, are common antecedents. Although acute hemorrhagic leukoencephalitis is a rare complication in the context of SARS-CoV-2 infection, it is potentially fatal, with few cases reported in the literature, and is associated with high morbidity and mortality and prominent imaging findings. Therefore, its proper and timely recognition is crucial (5).

The clinical manifestations of patients with acute hemorrhagic leukoencephalitis usually occur between 15 and 30 days after the onset of respiratory symptoms. Approximately 78% of patients experience confusion, lethargy, difficulty walking, and other motor deficits. In cerebrospinal fluid studies, 70% of samples show at least one marker of inflammation, such as pleocytosis, hyperproteinorraquia, or oligoclonal bands (6).

As for radiological findings, CT scans usually show nonspecific alterations. However, microangiopathic white matter disease, acute and subacute nerve parenchyma infarcts, intracranial hemorrhages, encephalitis, and leptomeningeal enhancement have been described more frequently (1, 2). In the case presented, multifocal lesions are observed in the white matter, predominantly supratentorial (6), affecting both cerebral hemispheres, with a greater predilection for the parietal and occipital lobes. These lesions are not easily identifiable on CT, as they may appear as nonspecific supratentorial low-density areas. However, on T2-weighted MRI sequences, they usually appear as areas of high signal intensity, without restriction on diffusion sequences, while on T1-weighted sequences they have low signal intensity, without gadolinium enhancement, indicating areas of cerebral edema. In addition, foci of microhemorrhage can be identified on ferromagnetic susceptibility sequences (SWI) (5). Less frequently, lesions may involve the gray matter of the cerebellar peduncles, the brainstem, and the basal ganglia, as in the case described (7). Regarding spinal involvement, a systematic review conducted in 2021 concluded that approximately half of patients suffer from spinal cord abnormalities; the most common are focal myelitis lesions, followed by longitudinally extensive myelitis (6). Widely distributed foci of microhemorrhages and brainstem involvement are imaging findings associated with a worse prognosis (5).

Regarding treatments, the use of corticosteroids and immunoglobulins is suggested. However, despite timely detection and management, acute hemorrhagic leukoencephalitis remains a pathology with high morbidity and mortality (6).

Conclusion

A case of acute hemorrhagic leukoencephalitis, a potentially fatal and rare subtype of ADEM associated with SARS-CoV-2 infection, was documented with typical imaging findings, which are very useful for establishing the diagnosis.

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