Posterior Reversible Encephalopathy Syndrome in COVID-19 Disease: a Case-Report

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Abstract
Posterior reversible encephalopathy syndrome (PRES) is a clinical syndrome that can include headache, altered consciousness, visual disturbances, and seizures, usually related to autoregulatory cerebral failure and hypertension. The neuroimaging is essential to diagnosis, showing white matter vasogenic edema in posterior areas. We present a case of a 66-year-old woman with severe pneumonia by SARS-CoV-2 who developed a posterior reversible encephalopathy syndrome with a typical clinical and radiological presentation, after being treated with anti-interleukin treatment (anakinra and tocilizumab) following local guidelines. We report a case of posterior reversible encephalopathy syndrome in a patient with COVID-19 disease, possibly related to anti-IL-1 or anti-IL-6, suggesting that anti-interleukin treatments may cause this syndrome, at least in patients with predisposing conditions such as infections and hydroelectrolytic disorders.

Keywords Posterior reversible encephalopathy syndrome (PRES) · COVID-19 · Anakinra · Tocilizumab · Immunomodulators

Introduction
A 66-year-old woman with COVID-19 presented with adult respiratory distress syndrome (ARDS). Besides bilateral pneumonia, she developed multiple complications such as cardiorespiratory arrest, bacterial superinfection, hyponatremia, massive hemoptysis requiring embolization, and acute renal injury. She was started on lopinavir/ritonavir, hydroxychloroquine, and azithromycin. After radiological pulmonary progression, anti-IL-1 (daily anakinra) and anti-IL-6 (single dose of tocilizumab) were started, following local and hospital guidelines. These drugs are recommended in COVID-19 when there is clinical, blood test, or radiological progression, to avoid an excessive immunological systemic response to the virus, which is thought to worsen pulmonary infiltrates and disease prognosis. Ten days after the initiation of immunodepressants, she developed altered mental status without fever, previous headache, or visual disturbances.

Case Presentation
At the examination, the patient opened eyes to painful stimuli, had no verbal response, and showed withdrawal response to pain (Glasgow Coma Scale 7). The blood tests showed stable hyponatremia (130 mEq/L) and leukocytosis without any other significant findings. Her vitals were within normal limits, and blood pressure had been mildly increased during the previous 12 h with a maximum systolic pressure of 160 mmHg. Electrocardiogram showed sinus rhythm and had not atrioventricular node blocks. A CT scan with angiography was performed. There was no large vessel occlusion, no perfusion alterations, and the baseline CT (Fig. 1) showed temporoccipital white matter hypodensity with symmetric obliteration of the sulci in that region.

Considering the infectious background, the immunomodulatory treatments, modest hypertension in the hours before the symptoms, and the distribution of the lesions on the CT scan, the most likely diagnosis is posterior reversible encephalopathy syndrome (PRES) [1–5]. Hypertension plays a vital role in
The disease due to a failure in cerebral blood flow autoregula-
tion, and in this case, rapid rise or fluctuations in blood pres-
sure from baseline may have been harmful, despite not being
severely high [2]. The electroencephalogram showed focal
slowing and epileptiform discharges in both occipital areas
and ruled out nonconvulsive status epilepticus. The symp-
toms improved over the following days after tight control
of blood pressure with labetalol infusion and discontinuing
anakinra.

After 1 week, radiological infiltrates worsened and a blood
test showed increased acute phase reactants. In this context, a
diffuse alveolar hemorrhage was diagnosed by bronchoalve-
olar lavage, with suspicion of hemophagocytic syndrome. She
required red blood cell transfusions and immunosuppressants
were restarted, as well as mechanical ventilation. The CT pul-
monary scan showed worsening of infiltrates and presence of
an intrapulmonary hematoma. Finally, the patient had a torpid
evolution to multiorgan failure and death.

Conclusions

The absence of fever and radiological findings did not suggest
an encephalitic cause of the symptoms. The serum sodium
levels were only slightly decreased and had been stable for
the previous days without intravenous infusion of sodium.
Thus, hyponatremia was not assumed to be the cause of the
sudden loss of consciousness. The cardiorespiratory arrest
happened a month before the event while intubated, and it
was secondary to a mucus plug after a period of desaturation
and bronchospasm. It lasted less than 5 min and ended as the
mucus plug was removed by fibrobronchoscopy. The post-
anoxic cerebral damage was prevented by treating fever;
avoiding systemic hypotension, hypoxemia, or glycemic
disbalance; and continuing renal replacement therapy with
hemodiafiltration instead of hemodialysis to prevent large
changes in volemia. One week later, sedation was stopped
and a tracheostomy was placed, and the patient progressively
awakened up to a normal state of consciousness without focal
neurologic signs. The timeline and posterior complete
recovery from the respiratory arrest cannot explain the current
episode as hypoxic-ischemic encephalopathy.

PRES has been associated with immunosuppressive and
cytotoxic therapies such as platinum-containing drugs, (R)-
CHOP regimens, gemcitabine, cyclosporine, tacrolimus,
sirolimus, and interferon therapies. Also, agents that target
angiogenesis such as bevacizumab (anti-VEGF) and tyrosine
kinase inhibitors (TKI) against VEGF receptor (pazopanib,
sorafenib, sunitinib) have been described as risk factors [3,
4]. Prior exposure to the predisposing drug does not appear
to be protective, and patients can develop PRES even after
several months after exposure [2]. Furthermore, the disorder
has been associated with both acute and chronic renal disease,
as was the case in our patient, and medical conditions such as
hyponatremia or pulmonary infection could exacerbate the
neurological findings.

Despite not being described yet, the occurrence of PRES a
few days after anti-interleukin (IL-6 or IL-1) treatments which
were given in this patient, raises the possibility that these kinds
of immunomodulatory agents may also favor PRES.

Compliance with Ethical Standards

Conflict of Interest  The authors declare that they have no conflict of
interest.

Ethical Approval and Informed Consent  Consent for publication was
obtained from the next of kin (daughter). Approval from the Hospital’s
IRB was provided for this study.

References

1. Fugate JE, Claassen DO, Cloft HJ, Kallmes DF, Kozak OS,
Rabinstein AA. Posterior reversible encephalopathy syndrome: as-
associated clinical and radiologic findings. Mayo Clin Proc. 2010;85:
427–32.
2. Gao B, Lyu C, Lerner A, McKinney AM. Controversy of posterior
reversible encephalopathy syndrome: what have we learnt in the last
20 years? J Neurol Neurosurg Psychiatry. 2018;89:14–20.
3. Allen JA, Adlakha A, Bergethon PR. Reversible posterior leukoencephalopathy syndrome after bevacizumab/FOLFIRI regimen for metastatic colon cancer. Arch Neurol. 2006;63:1475–8.

4. Ito Y, Arahata Y, Goto Y, et al. Cisplatin neurotoxicity presenting as reversible posterior leukoencephalopathy syndrome. AJNR Am J Neuroradiol. 1998;19:415.

5. Schwartz RB, Jones KM, Kalina P, Bajakian RL, Mantello MT, Garada B, et al. Hypertensive encephalopathy: findings on CT, MR imaging, and SPECT imaging in 14 cases. AJR Am J Roentgenol. 1992;159:379–83.

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