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COMMENTARY

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Respiratory failure alone does not suggest central nervous system invasion by SARS-CoV-2

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Many viruses can occasionally gain entry into the human central nervous system (CNS), even if most of the disease they cause does not involve the CNS. Although evidence of coronavirus (CoV) infection has been identified in children with encephalitis,[1] and nucleic acid of CoVs can be demonstrated in human brain,[2,3] isolation of infectious virus, or detection of virus by PCR in the context of a compatible clinical illness is only rarely reported the literature.[4] Human CoVs (HCoV) can infect CNS cell types in culture[5] and can cause encephalitis in newborn mice,[6] but despite this apparent biological basis for HCoVs causing CNS disease in humans, no definitive link between HCoVs and human nervous system disease has been made.[7]

Li et al[8] have proposed that severe acute respiratory syndrome (SARS)-CoV-2 can enter the brain, and this might be the cause of the respiratory failure seen in patients with COVID-19. They suggest that patients with COVID-19 need ventilation because they "cannot breathe spontaneously." However, this is likely not the case. Patients with pneumonia typically develop hypoxic, or type 1 respiratory failure, with low CO_2 levels and a raised respiratory rate. They can breathe spontaneously but the increased work of breathing in the face of poorly functioning lungs becomes too great to sustain. Artificial ventilation takes away the work of breathing from the patient until the lung has recovered sufficiently for the patient to breathe on their own. During ventilatory support, patients can often still initiate breaths, which are then supported by the ventilator. This is not suggestive of brain dysfunction. Brain failure leading to failure of breathing usually manifests as reduced respiratory rate, with low oxygen and high CO_2 due to ventilatory failure (type 2 respiratory failure). This may be accompanied by other signs of brain dysfunction. These are not reported to any great degree in any of the case series of patients from China.[9] The only case series of neurological symptoms reported to date mostly nonspecific symptoms that do not necessarily imply CNS disease,[10] although there was one report of ataxia and one of seizures, which is intriguing.

More convincing evidence of brain dysfunction caused by SARS-CoV-2 would include specific focal neurological defects, or type 2 respiratory failure (especially if it occurred with little in the way of lung disease) This should be accompanied by detection of virus in cerebrospinal fluid by PCR or, ideally, viral culture.

It remains plausible that SARS-CoV-2 can enter the CNS and cause disease in humans. But if so, this is a rare event. Although clinicians should be vigilant for CNS involvement with COVID-19, as they should be for any new disease, at present there is no good evidence that CNS disease occurs with SARS-CoV-2, nor is it frequent with any human coronavirus.

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