Severe Ebola Virus Infection With Encephalopathy: Evidence for Direct Virus Involvement

To the Editor—Major neurological signs are infrequent in Ebola virus (EV) disease. When present, they consist mainly of meningitis, encephalopathy, and seizures [1, 2]. The physiopathology of brain impairment in EV disease is not well understood. Here, we report the case of an EV disease patient with encephalitis and meningitis from whom cerebrospinal fluid (CSF) was obtained.

A 21-year-old man without any remarkable medical history was referred to our Ebola healthcare center with a 5-day history of severe febrile gastroenteritis and headache. At admission, the patient complained of diarrhea, vomiting, and abdominal pain and had signs of dehydration without neurological impairment or hemorrhagic symptoms.

Throughout his stay, the patient’s core body temperature was ≤38°C and his systolic blood pressure was >100 mmHg. He tested positive for EV (blood subjected to polymerase chain reaction; cycle threshold, 14.4); an immunochromatographic rapid test for malaria was negative. A routine blood panel revealed an elevated partial thromboplastin time (PTT) that was 4.4-fold the upper limit of normal values (ULN), an international normalized ratio (INR) of 1.9, a serum creatinine level of 173 μmol/L, and a high aspartate aminotransferase level (23-fold ULN). Twenty-four hours after being admitted, the patient worsened, exhibiting signs of hemorrhagic syndrome onset (ie, including hematuria, hemoptysis, and bleeding gums) and demonstrating an INR that had increased to 2.9. He was given 4 units of French lyophilized plasma. The next day, the patient was stuporous with nuchal stiffness and seizures but remained without focal neurologic signs. A lumbar puncture performed to test for bacterial meningitis revealed sterile CSF with no red or white blood cells. The patient’s viral load was 10⁵ copies/mL CSF and 6 × 10⁹ copies/mL blood. His blood and CSF glucose levels were both 3.7 mmol/L. Proteinoracia could not be assessed due to the lack of an appropriate device. The patient died within 24 hours of the lumbar puncture. A few hours before the patient died, biologic analyses disclosed coagulopathy with a normal platelet count (PTT, 7.2-fold ULN; INR, 6.2), renal impairment (high serum creatinine [234 μmol/L] and urea [10.1 mmol/L]), and hyponatremia (130 mmol/L).

The demonstration of a detectable CSF viral load in this case indicates that EV can cross the blood-brain barrier and thus may have a pathogenic role in the onset of encephalitis. In this case, there was no evidence of metabolic impairment such as hyponatremia or acute renal/hepatic encephalitis. The absence of focal neurologic signs and of red blood cells in the patient’s CSF ruled out a significant brain hemorrhage. EV-related physiopathology of the brain has not been characterized. In cynomolgus macaques, EV has a ubiquitous distribution, infecting endothelial cells of all organs, including brain venules and capillaries, from the fifth day of infection onward [3]. Necropsy, immunohistochemistry, and in situ hybridization findings have thus far been unremarkable in nonhuman primates up to 6 days after infection. However, our patient showed signs of encephalopathy 7 days after the onset of symptoms [4]. Edema and widespread glial nodules suggestive of encephalitis have been documented previously in human patients infected with the Marburg virus, another filovirus, but not in EV-infected patients [5]. The findings of the present case report suggest that EV can exist in the brain and thus that the brain should be a target for EV treatment.

Notes

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