

4. Knauf WU, Lissichkov T, Aldaoud A, et al. Phase III randomized study of bendamustine compared with chlorambucil in previously untreated patients with chronic lymphocytic leukemia. *J Clin Oncol* 2009;27:4378-84.
5. Hillmen P, Robak T, Janssens A, et al. Chlorambucil plus

ofatumumab versus chlorambucil alone in previously untreated patients with chronic lymphocytic leukaemia (COMPLEMENT 1): a randomised, multicentre, open-label phase 3 trial. *Lancet* 2015;385:1873-83.
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Zika Virus Associated with Meningoencephalitis

TO THE EDITOR: Zika virus (ZIKV) is currently spreading widely, while its clinical spectrum remains a matter of investigation. Evidence of a

relationship between ZIKV infection and cerebral birth abnormalities^{1,2} is growing.³ An increased incidence of some peripheral nervous syndromes

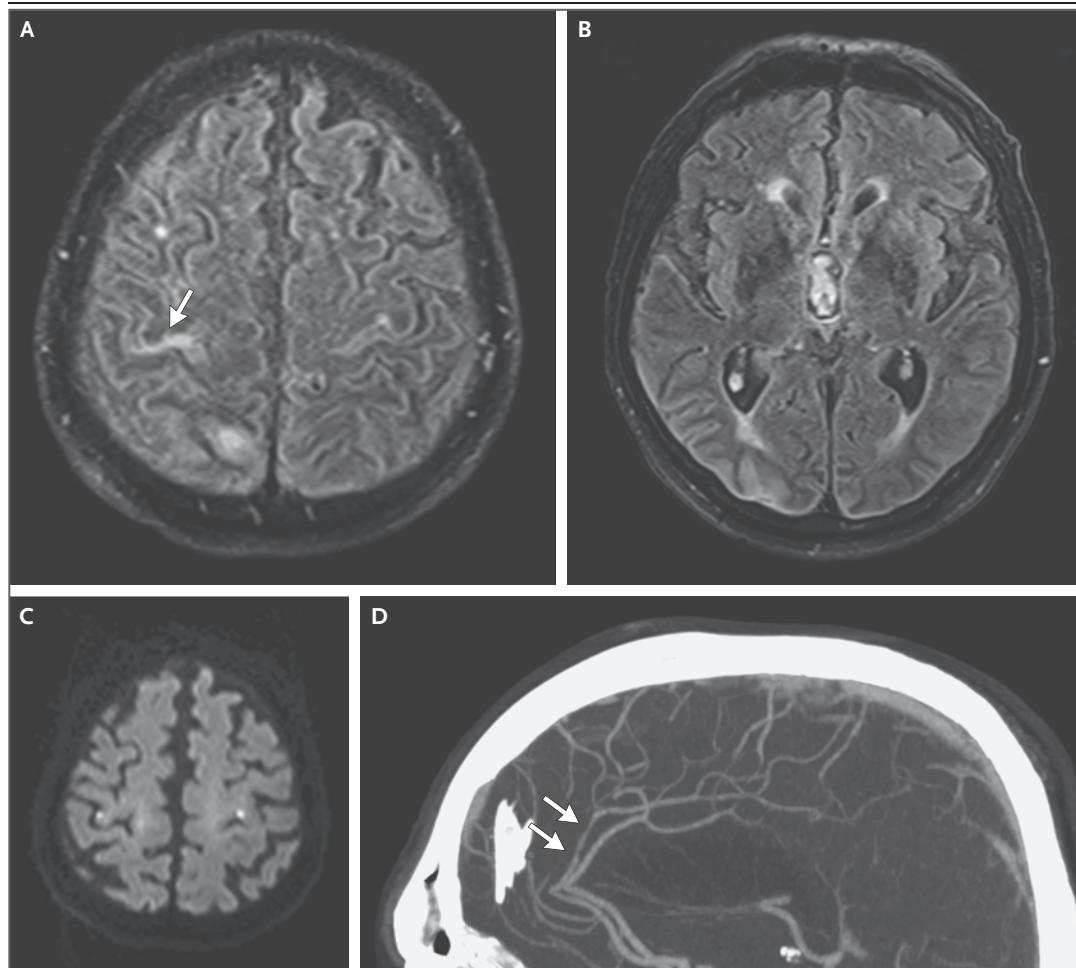


Figure 1. Imaging of the Brain.

MRI with the use of fluid-attenuated inversion recovery (FLAIR) imaging revealed subcortical white-matter hyperintensities in the right frontal region, the right temporo-occipital region (Panel B), and bilateral rolandic regions (Panel A). The slight hyperintensity of the right rolandic fissure (Panel A, arrow) is suggestive of meningitis. The multiple punctuated hyperintensities on diffusion-weighted sequences are suggestive of ischemic foci (Panel C). The MRI with FLAIR imaging and diffusion-weighted sequences were performed with the use of a 3T MRI unit (Magnetom Verio, Siemens). The computed tomographic angiogram shows an irregular narrowing of the right callosomarginal artery (Panel D, arrows). Angiography was performed with the use of a Discovery CT750 HD scanning system (GE Medical Systems).

among adults was reported during outbreaks in French Polynesia^{4,5} and Brazil,^{1,2} but no formal link with ZIKV infection was shown. We describe a case of central nervous system infection with ZIKV that was associated with meningoencephalitis in an adult.

An 81-year-old man was admitted to the intensive care unit (ICU) 10 days after he had been on a 4-week cruise in the area of New Caledonia, Vanuatu, the Solomon Islands, and New Zealand; he was reported to have been in perfect health during that time. On medical examination, he was febrile (39.1°C) and comatose (Glasgow Coma Scale score of 6 on a scale from 3 to 15, with lower scores indicating a reduced level of consciousness) with hemiplegia of the left side, paresis of the right upper limb, a normal response to tendon reflexes, and a Babinski sign on the left side. The patient's trachea was intubated and mechanical ventilation begun; a transient rash was observed within the next 48 hours.

Magnetic resonance imaging (MRI) of the brain was suggestive of meningoencephalitis. There were asymmetric subcortical white-matter hyperintensities on fluid-attenuated inversion recovery (FLAIR) imaging, multiple punctuated hyperintensities on diffusion-weighted sequences that were evocative of ischemic foci, and a slight hyperintensity of the right Rolandic fissure that was evocative of meningitis (Fig. 1). Computed tomographic angiography revealed an irregular narrowing of the right callosomarginal artery.

A lumbar puncture was performed on day 1, and findings on analysis of cerebrospinal fluid (CSF) were suggestive of meningitis: the leukocyte count was 41 per cubic millimeter (with 98% polymorphonuclear leukocytes), the protein level was 76 mg per deciliter, and the ratio of CSF to blood glucose was 0.75. The patient was initially treated with amoxicillin, cefotaxime, gentamicin, and acyclovir, but these antimicrobial agents were stopped on day 5. Investigations in both CSF and blood for other infections were unrevealing (see the Supplementary Appendix, available with the full text of this letter at NEJM.org), except for a positive result for ZIKV on reverse-transcriptase–polymerase-chain-reaction assay of the CSF (cycle threshold, 34). ZIKV was grown in culture from the CSF on a Vero cell

line (see the Supplementary Appendix). These findings all support the diagnosis of ZIKV-associated meningoencephalitis.

Several electroencephalograms showed no direct signs that were suggestive of epilepsy during levetiracetam therapy (which was administered for the first time in the ICU because seizure had been suspected as one of the mechanisms of the initial consciousness disorder). Spontaneous arousal occurred within 24 hours after intubation, and mechanical ventilation was weaned on day 2. At that time, the patient was awake but had spatial delusion with visual and kinesthetic hallucinations and a persisting weakness (2/5) of the left arm. His neurologic condition continued to improve without specific treatment. He was discharged from the ICU on day 17, and his cognitive function was fully recovered by day 38. He had a residual weakness (4/5) of the left arm. Clinicians should be aware that ZIKV may be associated with meningoencephalitis.

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1. Fauci AS, Morens DM. Zika virus in the Americas — yet another arbovirus threat. *N Engl J Med* 2016;374:601-4.
2. Latest Zika virus situation reports. Geneva: World Health Organization, 2016 (<http://www.who.int/emergencies/zika-virus/situation-report/en/>).
3. Mlakar J, Korva M, Tul N, et al. Zika virus associated with microcephaly. *N Engl J Med* 2016;374:951-8.
4. Iosifidis S, Mallet H-P, Leparac Goffart I, Gauthier V, Cardoso T, Herida M. Current Zika virus epidemiology and recent epidemics. *Med Mal Infect* 2014;44:302-7.
5. Oehler E, Watrin L, Larre P, et al. Zika virus infection complicated by Guillain-Barre syndrome — case report, French Polynesia, December 2013. *Euro Surveill* 2014;19.

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