Demyelinating Encephalitis
(See pages 1266–7 for Photo Quiz)

Figure 1. Left, T1-weighted MRI with gadolinium demonstrating multiple hypodense lesions in the deep white matter. Right, Fluid-attenuated inversion recovery MRI image of the same lesions. A movement artifact is present.

Diagnosis: Acute disseminated encephalomyelitis (ADEM).

The pathologic diagnosis was severe ADEM. The initial differential diagnosis for diffuse, nonhemorrhagic leukoencephalitis with multiple hypodense white-matter lesions (figure 1) included Marburg variant multiple sclerosis (MS), progressive multifocal leukoencephalopathy, postmeasles encephalomyelitis, gummatous neurosyphilis, leukoencephalitis due to Herpesviridae (cytomegalovirus or varicella zoster virus, more likely than herpes simplex virus), primary CNS lymphoma, severe HIV-associated leukoencephalopathy [1], atypical presentations of other infectious CNS lesions (including those due to infection with Mycobacterium tuberculosis, Cryptococcus neoformans, Toxoplasma gondii, or Taenia solium), and conditions of noninfectious etiology (such as metastatic neoplasms, autoimmune disorders, and vasculitis). On the basis of the pathologic findings (figure 2), the primary alternate diagnosis was Marburg variant multiple sclerosis.

The patient’s condition did not improve when he was treated with broad-spectrum, intravenous anti-infective agents (including ceftriaxone, ampicillin, doxycycline, acyclovir, and fluconazole), high-dose corticosteroids, or intravenous immunoglobulin (IVIG). After a 6-week hospitalization, the patient was discharged to a skilled nursing facility with severe but stable neurologic deficits.

ADEM can be a devastating disease. It occurs more commonly in children and young adults than in older adults. No standardized diagnostic criteria exist, but ADEM is typically a monophasic illness characterized by prominent neurologic deficits that resemble those of viral encephalitis or MS [2]. In fact, 35% of patients with ADEM may eventually have MS diagnosed [3]. CSF is normal in one-third of patients, but other patients may have mild mononuclear pleocytosis, elevated protein levels, and evidence of intrathecal oligoclonal IgG production [2]. It is important to note that lesions may not appear on an MRI until up to 2 weeks after the onset of symptoms [4].

ADEM probably results from an autoimmune reaction to myelin basic protein. This reaction is likely triggered by pathogen-associated antigens introduced by inoculation or infec-
tion. In the past, ADEM most commonly followed vaccinia or measles infections. More recently, it has been reported after administration of measles, mumps, and rubella vaccine [4]. Nonviral pathogens may also induce this immune-mediated demyelinating condition [5].

No controlled trials of treatment have been performed, but treatment with corticosteroids, IVIG, plasmaphoresis, and hypothermia may be beneficial. ADEM following measles has a mortality rate as high as 20%. By comparison, only 2 (8%) of 26 patients with ADEM died in a recent case series, although 12 (46%) survived with persistent neurologic deficits [3].

This case assumes particular importance in light of the national debate regarding the program for widespread vaccination against potential agents of bioterrorism. In 1968, smallpox vac-

Figure 2. A. Photomicrograph of a section of tissue from the temporal-lobe white matter lesion demonstrating intense perivascular macrophage infiltration (hematoxylin-eosin stain). B, Section of white matter demonstrating extensive demyelination that was worse near blood vessels (hematoxylin-eosin stain with luxol fast blue).
cination resulted in encephalitis at a rate of \( \sim 1 \) case per 300,000 doses, with a mortality rate of 25% and frequent neurologic sequelae in survivors [6]. The possibility of debilitating, vaccination-associated encephalitis should be considered when weighing the risks and benefits of large-scale immunizations.

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References


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