19 Demyelination

19.1 Acute Disseminated Encephalomyelitis (Postinfectious/Postvaccination Perivenous Encephalomyelitis)

Acute disseminated encephalomyelitis (ADEM) is a demyelinating disease that affects all ages, except children less than 2 years. It occurs during the course of various infections, particularly the acute exanthematous diseases of childhood (measles, rubella, chickenpox, and smallpox immunization), other common viral infections (i.e., Epstein-Barr virus, adenovirus, cytomegalovirus, influenza, rhinoviruses, coronaviruses), and following vaccination against smallpox, measles, and rabies. The clinical features are the same regardless of the inciting event. The symptoms develop days to weeks after the onset of the predisposing cause. The symptoms and signs of acute disseminated encephalomyelitis are related to the portion of the central nervous system (CNS) that is most severely damaged. Death occurs in 20%–30%. There are neurological deficits in survivors.

Pathology

The brain shows mainly involvement of the white matter with numerous small foci of demyelination. Histologically, there is a destructive inflammatory reaction with lymphocytes and occasional plasma cells around small veins throughout the cerebrum, brain stem, cerebellum, and spinal cord. Phagocytic microglial cells are present in the lesions. There is relative sparing of axons and nerve cells. There is a sharp margin between the foci of demyelination and normal areas. At later stages, the extent of gliosis exceeds the area of demyelination. In ADEM the tissue reaction is the same age everywhere reflecting the monophasic nature of the disease. This differs from multiple sclerosis in which lesions are of differing ages [1].

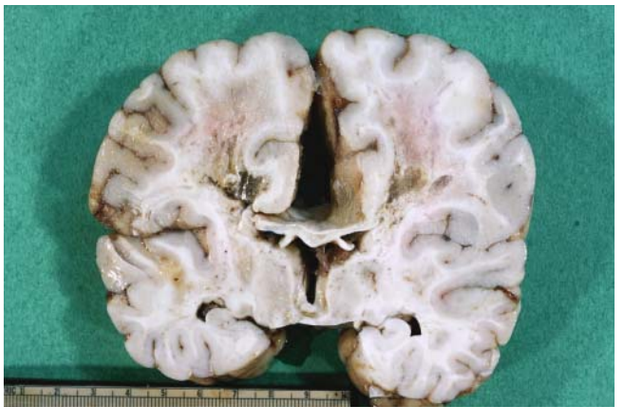

Fig. 19.1-1. ADEM. Multiple sites of demyelination in the white matter of the cerebrum.

Fig. 19.1-2. Multiple lesions of demyelination in the cerebellar white matter.

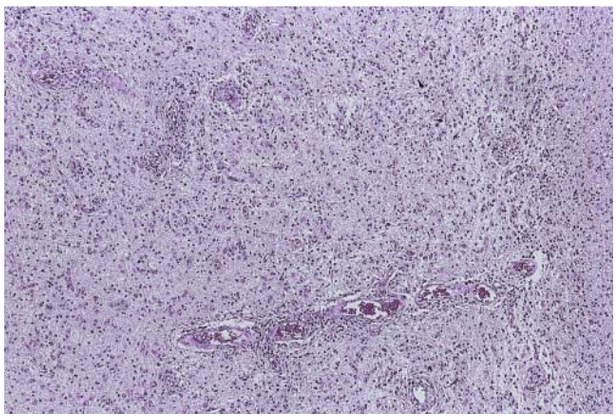

Fig. 19.1-3. Perivascular small round cell infiltration in the cortex and white matter. H&E.

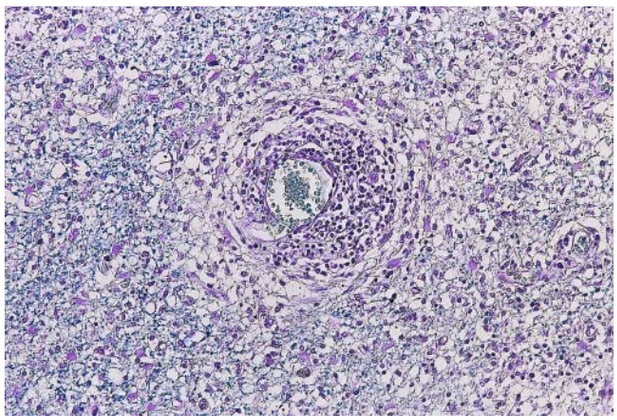

Fig. 19.1-4. Perivascular cuffing with astrogliosis and loss of myelin sheaths in the same case. LFB.

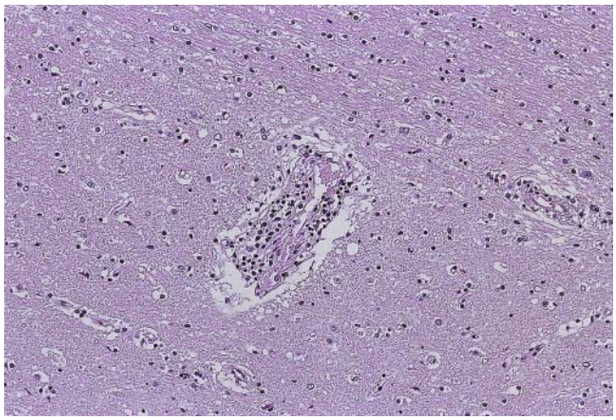

Fig. 19.1-5. Perivascular cuffing in the white matter in the same case. H&E.

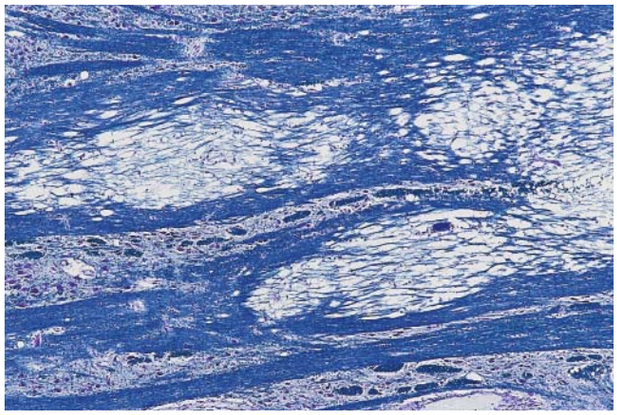

Fig. 19.1-6. Microscopic multifocal demyelination in the same case. LFB.

19.2 Acute Necrotizing Encephalopathy

Acute necrotizing encephalopathy (ANE) is a type of acute encephalopathy that affects young children following febrile viral diseases such as influenza and exanthema subitum [2]. ANE is most prevalent in East Asia but is also present in other regions of the world. The clinical course of ANE is fulminant, with a rapid decrease of consciousness, variable degrees of hepatic dysfunction, and severe neurological sequelae in the survivors [3].

Pathology

The lesions of ANE exhibit edema, petechial hemorrhage, and necrosis, suggesting local breakdown of the blood–brain barrier. Both the gray and white matter are involved. The parenchymal lesions have a laminar pattern surrounding vessels, which exhibit excessive permeability, producing an area of "vasogenic edema." This increases, moving deep into the brain away from the cerebral surface [4].

Magnetic Resonance Imaging

Cranial computed tomography (CT) and magnetic resonance imaging (MRI) show characteristic bilateral brain lesions in which the multiple, symmetrical brain lesions affect the bilateral thalami, putamina, cerebral periventricular white matter, cerebellum, and brain stem tegmentum. Images of the lesions often exhibit a concentric structure, such as is seen in the tissue pathology. The periphery of the lesions shows positive contrast enhancement [4].

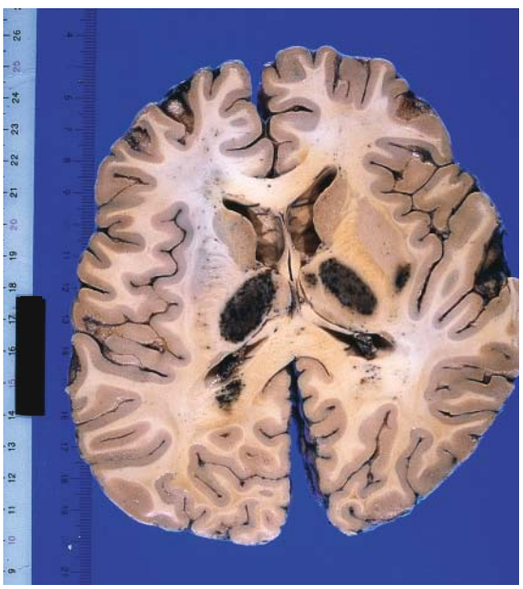

Fig. 19.2-1. Acute necrotizing encephalopathy (ANE). Note the cavity formation with hemorrhagic necrosis in the thalamus and white matter of both cerebral hemispheres. (Courtesy of Dr. Mizuguchi M.)

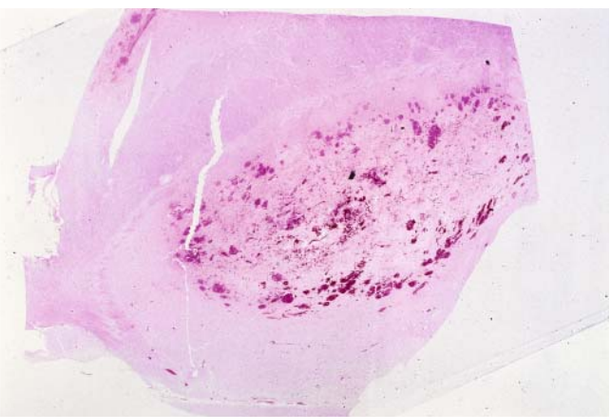

Fig. 19.2-2. Whole mount of thalamus shows a focus of hemorrhagic necrosis. H&E.

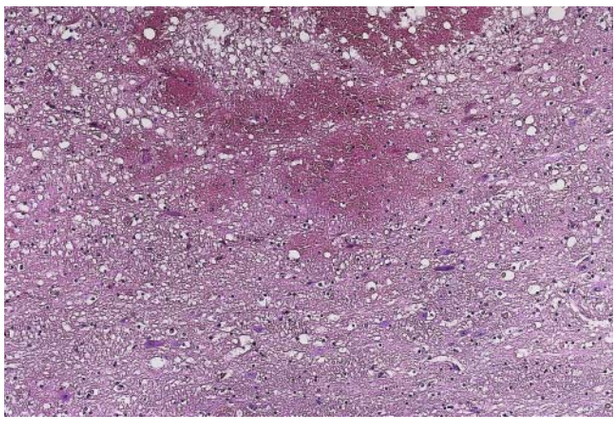

Fig. 19.2-3. Hemorrhage and necrosis in the thalamus. H&E.

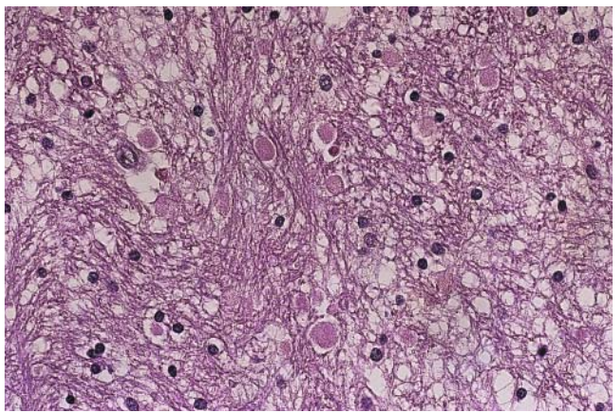

Fig. 19.2-4. Axonal swelling in white matter. H&E.

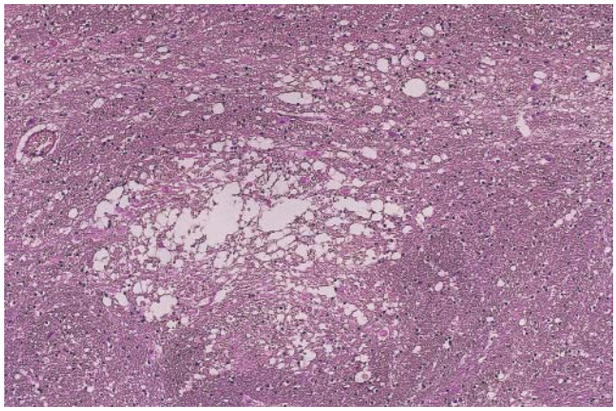

Fig. 19.2-5. Focal necrosis with spongy changes in white matter. H&E.

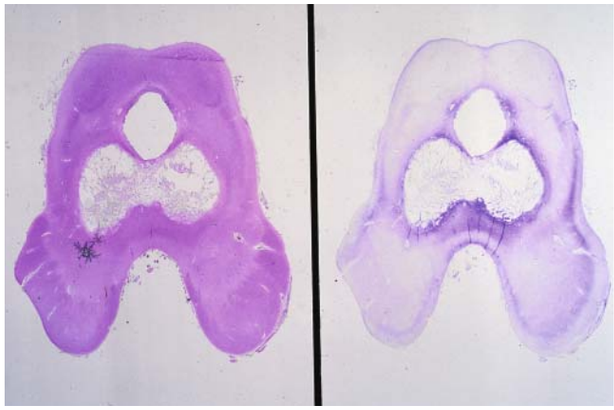

Fig. 19.2-6. Cystic necrosis in the midbrain tegmentum. *Left*. H&E. *Right*. Holzer stain.