Acute necrotizing hemorrhagic leukoencephalitis

By Anthony T Reder MD (Dr. Reder of the University of Chicago served on advisory boards and as a consultant for Bayer, Biogen, Caremark Rx, Genzyme, Novartis, Questcor, Serono, and Teva-Marion.)

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**Introduction**

This article includes discussion of acute necrotizing hemorrhagic leukoencephalitis, acute hemorrhagic encephalitis, acute hemorrhagic leukoencephalitis, acute necrotizing hemorrhagic encephalomyelitis, and acute necrotizing hemorrhagic encephalopathy. The foregoing terms may include synonyms, similar disorders, variations in usage, and abbreviations.

**Overview**

Acute hemorrhagic leukoencephalitis of Weston Hurst is at the extreme end of the spectrum of demyelinating diseases. It typically follows a viral upper respiratory infection and evolves rapidly to coma and death. "Ball and ring" hemorrhages appear in the centrum semiovale of the brain, associated with mononuclear and neutrophil infiltrates, surrounded by demyelination spreading out from fibrin-filled venules. In this article, the author addresses these issues and suggests that IL-17, a cytokine that attracts neutrophils, may be important in pathogenesis.

**Key points**

- Acute necrotizing hemorrhagic leukoencephalitis is a devastating disorder that often follows a virus or mycoplasma infection.
- Lesions are hemorrhagic, with fibrinoid necrosis and polymorphonuclear neutrophil infiltration that is associated with demyelination.
- The devastating immune response is from excess sensitization to 1 or more unknown antigens.
- Therapy is difficult, and most of those affected will die. Several therapies are suggested to deactivate the immune response.

**Historical note and terminology**

E. Weston Hurst was the first to clearly define acute necrotizing hemorrhagic leukoencephalitis and to suggest that it was a demyelinating disease (Hurst 1941). He described the abrupt onset of neurologic symptoms following a nonspecific upper respiratory infection in 3 patients: a 43-year-old housewife, a 33-year-old munitions worker, and a 37-year-old accountant. Death occurred in several days, and autopsies of 2 of these patients showed identical hemorrhagic lesions in the white matter. Other authors, such as Gayet, Leyden, Strümpell, Bückler, Leichtenstern, Brie, Oppenheim, de Faro, Baker, and Levy, described similar encephalitic conditions with petechial hemorrhage and inflammation, as early as 1875 (Lander 1958). More cases were detailed in the 10 years after the 1941 report (Adams et al 1949; Crawford 1954).

**Clinical manifestations**

**Presentation and course**

The onset of acute hemorrhagic leukoencephalitis is abrupt and sometimes violent. It appears from 2 days to 2 weeks after a 3 to 5 day premonitory illness. It is most common in fall and winter. Viral upper respiratory infections are the most common antecedent (32%), but there is sometimes no prodrome (18%) (Geerts et al 1991). In one third of cases, the upper respiratory infection may be followed by a symptom-free period of several days, but neurologic symptoms then suddenly appear. Patients with acute myeloid leukemia in hematologic remission may be particularly susceptible (2%) to this rare condition (Pagano et al 1999). The most common ages are 20 to 40 years, but children and sexagenarians have been affected.

The course is brief and usually ends in death. Fever up to 106°F, headache, photophobia, neck stiffness, meningeal irritation, confusion, and lethargy last several days and are followed by a progressively deepening coma over 4 to 10 days (Lander 1958). A biphasic course over several weeks is possible. In one case of biphasic disease, high-dose steroids were withdrawn before the second episode (Pinto et al 2011), possibly leading to recrudescence. Neurologic
signs are protean because of the diffuse and massive necrosis of CNS white matter. Visual field disturbances, gaze preferences, pseudobulbar palsy, aphasia, or mutism suggest a cortical disturbance but actually arise from undercutting of the cortical connections by the white matter lesions. Progressive motor and sensory disturbances and incontinence appear early. Reflexes are usually hyperactive and toes are upgoing. Fifty percent of patients have hemiparesis. A smaller percentage has seizures or status epilepticus, involuntary movements, and dysarthria (Geerts et al 1991; Gogus et al 1991; Hafler 1995). Papilledema, a manifestation of increased intracranial pressure, is present in one third (Geerts et al 1991). Death results from brain swelling with herniation. Rarely, patients have a subacute course and rarely, they recover completely. CSF pleocytosis resolves after several weeks (Leake et al 2002), and clinical symptoms improve over weeks to months.

**Prognosis and complications**

Most patients (68%) die within a week of onset of neurologic symptoms (Geerts et al 1991). Survivors usually have severe deficits, including seizures, psychiatric symptoms, and mental deterioration. A few patients have recovered completely (Seales and Greer 1991; Leake et al 2002; Ryan et al 2007).

**Clinical vignette**

A 28-year-old life insurance salesman had an upper respiratory infection that resolved after 4 days. One week later, he developed a stiff neck, fever to 102°F, headache, and confusion. Left arm and leg weakness was followed by bilateral paresis, incontinence, dysarthria, and lethargy over the next 2 days. He was diffusely hyperreflexic and had bilateral papilledema.

His complete blood count showed 38,000 cells/mm3 with neutrophilia. There was a suggestion of diffuse hypodensity of the right hemisphere on CT scan. Spinal fluid showed an opening pressure of 345 mm H2O, 150 RBC/mm3, 3000 WBC/mm3 (largely polymorphonuclear leukocytes), total protein of 200 mg/100 ml, normal glucose, and no oligoclonal bands.

The symptoms and signs worsened over the next 4 days, and the patient became comatose 5 days after the onset of symptoms. Despite intravenous mannitol and high dose glucocorticoids, the patient expired 3 days later from herniation.

**Biological basis**

**Etiology and pathogenesis**

Most cases follow or overlap with a banal upper respiratory tract infection. Other prodromes occasionally lead to acute hemorrhagic leukoencephalitis: viral pneumonia, chickenpox, Epstein-Barr virus infection, HSV, VZV, HHV-6, measles, influenza, mycoplasma pneumonia infection, tuberculosis, minor operations, dental extraction, skin burns, chronic nephritis, relapses of ulcerative colitis (Byers 1975; An et al 2002), or vaccinations such as typhus, smallpox, cholera, dysentery, hepatitis B (Konstantinou et al 2001), and pneumococcal polysaccharide. Scattered reports attribute a kindred disease to toxins and drugs (arsphenamine) (Graham et al 1979). Three cases have followed treatment of tuberculosis (Chetty et al 1997). This suggests that components of mycobacterium tuberculosis activated the immune system, just as when mycobacterium tuberculosis is used to create complete Freund adjuvant for induction of experimental autoimmune diseases.

At autopsy the brain is edematous and swollen. The tissue is pink or yellow-gray, with diffuse petechial hemorrhages and congested vessels, and may approach a state of liquefaction (Hurst 1941; Lander 1958; Geerts et al 1991; Vartanian 1999). The centrum semioule is the main area affected, often asymmetrically. Microscopic changes include diffuse edema, widespread areas of demyelination and fibrinoid necrosis. There is perivenous inflammation around blood vessels in the brain and in the meninges, with microglial foci and infiltrating polymorphonuclear cells and activated mononuclear cells. Small hemorrhages abound in the centrum semiovale, but massive hemorrhage is
atypical. The pons and cerebellar peduncles also sometimes contain small hemorrhages.

The sequence of events begins with swollen endothelial cells, continues with plasma leakage into the CNS, and is followed by cellular infiltrate (first neutrophils, then macrophages, and finally lymphocytes). Capillaries are disrupted with a surrounding hemorrhagic ball that forms a ring (“ball and ring”) around a bloodless center that sometimes contains a fibrin clot. The walls of venules are impregnated or replaced with fibrin, often extending into the perivascular space and brain tissue. This is not a necrotizing angiitis because initially there is no inflammation of the vessels (and small venules instead of arterioles are involved). It would be better termed an angioopathy. The cause of the endothelial cell necrosis is unknown, but possible etiologies include antibody-antigen-complement, toxic cytokines, or reactive oxygen intermediates (Vartanian 1999).

Demyelination predominates around small vessels that are surrounded by neutrophils. Some lymphocytes and lipid-filled macrophages are present, but most importantly, a neutrophilic infiltrate characterizes acute hemorrhagic leukoencephalitis. Demyelinated areas contain activated microglia. Meninges may be infiltrated with lymphocytes (An et al 2002). Axonal damage is also dramatic. Beta-amyloid precursor protein, a marker for acute axonal damage, is present in axons and neuronal cell bodies surrounding inflamed veins (Ghosh et al 2004). Damaged axons are rare beyond 0.25 mm from the wall of the inflamed vessels. Macrophages are located in areas of axonal damage, suggesting macrophages cause the damage.

Cerebral white matter is the target. Early investigators implicated infection, toxins, and acquired sensitivity of brain tissue to a circulating antigen (Lander 1958). However, no infection or toxin is consistently associated, and pathogens are not present in the CNS.

A single report shows marked lymphocyte proliferation to myelin basic protein (Behan et al 1968), similar to that seen in the possibly related condition, acute disseminated encephalomyelitis. The kinetics of the anti-myelin basic protein response have not been studied. This group also used passive transfer of white blood cells from a patient with acute hemorrhagic leukoencephalitis to induce experimental allergic encephalomyelitis in monkeys (Behan and Lamarche 1969).

The pathology of the disease is reminiscent of hyperacute experimental allergic encephalomyelitis, provoked by vaccination with spinal cord homogenate in complete Freund’s adjuvant followed by pertussis toxin. Experimental allergic encephalomyelitis becomes hyperacute and similar to acute hemorrhagic leukoencephalitis when animals are exposed to intravenous meningococcal toxin (ie, when a Shwartzman reaction is superimposed on the response) (Waksman and Adams 1957). This suggests that sensitization to CNS antigens is enhanced by endotoxin. In support of this hypothesis, acute hemorrhagic leukoencephalitis can be provoked by Gram-negative septicemia that is associated with acute tubular necrosis and disseminated intravascular coagulation (Graham et al 1979).

In another relevant model, C57BL/6 mice are normally resistant to Theiler virus-induced demyelination because of their strong antiviral responses. However, if the main immune target protein is injected after 7 days of controlled virus infection, the blood-brain barrier opens and there is demyelination and microhemorrhages (Pirko et al 2008).

The predominance of neutrophils in acute hemorrhagic leukoencephalitis argues for elevated levels of IL-17, which attracts neutrophils. This proinflammatory cytokine is secreted by CD8 T cells and by a subset of CD4 memory T cells. IL-17-secreting CD4 cells are a separate lineage from Th1 and Th2 cells. Bacterial infection, lipopolysaccharide, and cytokines induce IL-17. Interleukin-6 plus transforming growth factor-beta generate IL-17-producing cells from naive CD4 cells. Interleukin-23 maintains this population and induces IL-17 in memory CD4 cells. IL-4, and also interferon-gamma and interferon-beta, inhibit IL-17 production. The IL-17 cytokine raises levels of IL-6 and granulocyte-colony stimulating factor that stimulate granulopoiesis in bone marrow, and induces chemokines (IL-8) that attract neutrophils.

Th-17 cells amplify CNS inflammation. They increase during exacerbations and are higher in CSF than serum (Matusevicus et al 1999). IL-17 is increased in plaques, CSF, and serum in neuromyelitis optica (Ishizu et al 2005). IL-17 has not been studied in acute hemorrhagic encephalomyelitis. Type I (alpha and beta) and II (gamma) interferons inhibit generation of IL-17-producing cells (Harrington et al 2005), so interferon-beta is a potential therapeutic agent, at least at the early stages of disease. A monoclonal antibody directed at IL-17 could also block the immune activation.

Two unrelated pediatric patients of Filipino descent with a partial complement factor I deficiency had upregulation of
complement C3, membrane attack complex, and IL-1 in the brain (Broderick et al. 2013). They improved after treatment with anti-IL-1 antibody. F1 is a serine protease that inactivates C3b and C4b. Complement and IL-1 may thus play a role in Hurst disease.

**Epidemiology**

Most early reports were from the United Kingdom and Australia. Subsequent descriptions originated in the United States, Belgium, France, Germany, Eastern Europe, Turkey, and Japan. Men are affected twice as frequently as women (Geerts et al. 1991). Approximately 100 case reports describing this rare disease are in the literature.

**Prevention**

No means of prevention are known.

**Differential diagnosis**

Other types of encephalitis are most likely to be confused with acute hemorrhagic leukoencephalitis. It must be separated from diseases that cause multiple petechial hemorrhages or multiple areas of demyelination.

**Demyelinating disorders.**

**Acute disseminated encephalomyelitis.** Acute disseminated encephalomyelitis also follows upper respiratory infections, and the inflammation is perivascular. However, hemorrhagic necrolysis is not present or is minimal, the peripheral white blood cell count is lower, and polymorphonuclear cells are not elevated in acute disseminated encephalomyelitis. In addition, acute disseminated encephalomyelitis lesions do not form large foci, cerebral edema is uncommon, and there is less axonal damage (Ghosh et al. 2004). T cells are sensitive to myelin basic protein in acute disseminated encephalomyelitis (Tselis and Lisak 1998). In the CSF, lymphocytes predominate (not neutrophils), and cells are present at lower levels. Protein is less elevated, opening pressure is lower, and oligoclonal bands are absent. Argument persists whether these are 2 separate entities or part of a spectrum, with acute hemorrhagic leukoencephalitis being the most rapidly developing form, and acute disseminated encephalomyelitis being a later form where recovery is much more likely (Leake et al. 2002).

In 84 Argentinean children, MRI showed 4 subgroups of acute disseminated encephalomyelitis with small lesions (62%), with large lesions (Schilder disease, 24%), with predominant bithalamic involvement (acute necrotizing encephalopathy, 12%), and acute hemorrhagic encephalomyelitis (2%) (Tenembaum et al. 2002). In a large series of Turkish children, one third had 1 or more relapses after the initial event. Prognosis was good; 71% recovered completely (Anlar et al. 2003). On MRI, lesions of acute hemorrhagic leukoencephalitis are larger and more edematous and often spare the basal ganglia (Kuperan et al. 2003).

**Acute necrotizing encephalopathy (ANE).** Acute necrotizing encephalopathy of childhood is described in children from the Far East (Japan, Korea, and Taiwan) and occasionally in the Occident (Turkey, Greece, Germany, and Canada) (Mizuguchi 1997; Yoshikawa et al. 1999). It causes bilateral, multifocal, symmetric destruction of thalamus, sometimes with a target appearance on MRI. In some cases there are also symmetric lesions in internal capsule, brainstem tegmentum, and cerebellum. Encephalopathy and seizures are typical. There are reports of several Japanese adults with this disorder. It is often preceded by viral infections (especially influenza A, H1N1; possibly HHV6, parainfluenza, and reovirus) by only 0.5 to 3 days, differentiating it from post-infectious encephalomyelitis, which typically develops 10 to 14 days after the infection. Cases have similar courses with or without antecedent influenza. Cytokine storm was reported in 1 patient. Another case associated with hemophagocytic lymphohistiocytosis suggests there is excessive immune system and macrophage activation. Many affected children had been treated with antipyretics. Steroids may be helpful.

Occasional cases have mutations in the nuclear pore protein Ran binding protein 2 (RANBP2) involved in neuronal energy metabolism. There may be a family history of similar recurrent events (“ANE1”) (Neilson 2010; Wolf et al. 2013). Lesions are more widespread and can include spinal cord lesions. Sodium channel alpha1 subunit (SCN1A) mutation was present in 1 case. Influenza also causes encephalopathy with cortical lesions, such as hemorrhagic shock and encephalopathy (HSES), acute brain swelling (ABS), and febrile convulsive status epilepticus (FCSE).

This monophasic disorder is associated with seizures (40%), acute encephalopathy with decreased consciousness
(30%), and vomiting (20%). Within 24 hours, diencephalic and upper brainstem damage causes spasticity, decerebrate posturing, mictic pupils, and coma. Liver enzymes are elevated by the second hospital day, but serum ammonia is normal. There are no infiltrating inflammatory cells, nor CSF pleocytosis. Lesions are usually symmetric. They are often hemorrhagic and cavitory and are found in the thalamus (essential for diagnosis), internal capsule, basal ganglia, brainstem tegmentum, and cerebral and cerebellar white matter. On T1-weighted MRI, bilateral thalamic lesions have a hyperdense center and a hypodense ring; densities reverse on T2-weighted MRI (Mizuguchi and Takashima 2002). The apparent diffusion coefficient (ADC) on MRI is decreased, whereas it is high in acute disseminated encephalomyelitis. The outcome is poor to grave.

**Multiple sclerosis.** Multiple sclerosis is seldom this fulminant and is less widespread in the brain. The reaction to myelin basic protein in multiple sclerosis is absent or minimal, in contrast to the strong response to myelin basic protein that is common in acute disseminated encephalomyelitis and also occasionally seen in acute hemorrhagic leukoencephalitis. Multiple sclerosis is typically recurrent, whereas acute hemorrhagic leukoencephalitis is monophasic, with the exception of one report (Lamarche et al 1972).

There are case reports of an association with Crohn disease or ulcerative colitis.

**Infections.**

**Bacterial meningitis.** Bacterial meningitis causes an early fall in CSF glucose. Polymorphonuclear cells are present in the spinal fluid, but red cells are not as common. Abundant bacteria are usually detected on Gram stain. Asymmetric changes in the white matter are uncommon. It is critical to differentiate meningitis from acute hemorrhagic leukoencephalitis because glucocorticoids are used to treat leukoencephalitis and antibiotics with or without steroids are used for meningitis.

**Bickerstaff brainstem encephalitis.** Sometimes caused by autoantibodies.

**Brain abscess.** Brain abscess is usually focal and is easily diagnosed with CT or MRI.

**Epidural empyema.** Epidural empyema is relatively rare at present. It is usually caused by sinus infection or trauma to the cranium that allows bacterial ingress.

**Eastern equine encephalitis.** Eastern equine encephalitis is a rare disease seen mostly in infants and children during late summer. It causes diffuse encephalitis with blood and spinal fluid pleocytosis.

**Hemorrhagic encephalitis of Baker.** The so-called hemorrhagic encephalitis of AB Baker did not follow upper respiratory infections, and not all of the white matter lesions were hemorrhagic. These distinctions seem trivial, and the condition is probably identical to acute hemorrhagic leukoencephalitis.

**Herpes simplex encephalitis.** Herpes simplex encephalitis is often focused in the temporal lobes. It evolves over days to a week. The peripheral white blood cell count is not as markedly elevated and the CSF infiltrate is lymphocytic instead of polymorphonuclear. Bloody CSF can be seen in both. Petechial hemorrhages are early in hemorrhagic leukoencephalitis, but appear later in herpes encephalitis. CT and MRI changes predominate in the temporal lobes, may enhance contrast, and white and gray matter are both involved in herpes encephalitis, rather than predominantly white matter. EEG changes are also common in the temporal lobes with herpes infection.

**Rasmussen encephalitis.** Rasmussen encephalitis has a much longer and slower course and is often unilateral.

**Other viruses.** Other viruses linked to this disorder include Epstein-Barr and influenza.

**Vascular disorders.**

**Brain purpura.** Brain purpura (pericapillary encephalorrhagia) is a noninflammatory condition with multiple small petechial hemorrhages and hyaline or fibrin clots obliterating the lumens of pre-capillary arterioles in the white matter (Hurst 1941). Patients develop stupor and coma, usually without focal signs. The CSF is normal. Its etiology is obscure, but it is sometimes associated with Gram-negative infections or with arsenic or phosgene poisoning. A combination of brain purpura and acute disseminated encephalomyelitis, perhaps the superimposition of one condition on the other, may be the etiology of acute hemorrhagic leukoencephalitis.
Cerebral venous thrombosis. Cerebral venous thrombosis causes seizures and focal cortical signs, especially from gray matter damage, in contrast to the centrum semiovale lesions in acute hemorrhagic leukoencephalitis.

Subarachnoid hemorrhage. Subarachnoid hemorrhage is explosive in onset and is associated with a severe headache and stiff neck. Focal or generalized neurologic signs can progress to death within hours to days.

**Toxic disorders.**

**Acute lead encephalitis.** Acute lead encephalitis may develop abruptly and sometimes generates focal signs and elevated CSF protein. Lead lines in the shafts of the long bones and a history of pica are common, usually in young children who ingest paint that contains lead.

**Arsphenamine encephalitis.** Arsphenamine encephalitis has a similar pathology (Adams et al 1949).

**Central pontine myelinolysis.** Central pontine myelinolysis follows abrupt electrolyte fluctuations. It causes demyelination with sharp borders, axonal damage, plus edema, macrophage inflammation, and astrocytosis. The axonal retraction bulbs and beta-amyloid precursor staining are not perivenular and the damaged axons are of larger diameter than in acute hemorrhagic encephalomyelitis (Ghosh et al 2004). Macrophage location does not correlate with axonal damage as would be expected with a metabolic, compared to an inflammatory, insult.

**Toxic spongiform encephalopathy.** Reversible toxic spongiform encephalopathy can follow inhalation of heated heroin vapor, or “chasing the dragon.” There is cerebellar ataxia, motor restlessness, and apathy. This is associated with bilaterally symmetric MRI lesions in cerebellar nuclei and white matter, deep cerebral white matter, and brainstem.

**Reye syndrome.** Reye syndrome is a mitochondrial disorder in children that follows use of aspirin during viral infections. Acute brain swelling is associated with protracted vomiting and hepatic damage.

**Subacute leukoencephalopathy.** Subacute leukoencephalopathy can follow chemotherapy.

**Wernicke encephalopathy.** Ataxia, ophthalmoparesis, and encephalopathy often with thiamine deficiency in alcoholics can have acute or subacute onset.

**Diagnostic workup**

The peripheral white blood cell count is markedly elevated, which is a rare finding in most other demyelinating conditions. Neutrophils predominate and range from 11,000 to 120,000 cells/mm3. The sedimentation rate is occasionally elevated.

The CSF is normal in 10%, usually early in the disease. Intracranial pressure is increased up to 350 mm H2O. CSF pleocytosis is from 10 to 4000 cells/ml, and rarely up to 20,000. There is usually a marked polymorphonuclear cell pleocytosis. Xanthochromia and red blood cells are often present and up to 150 cells/ml. The CSF total protein is elevated (one fourth have levels over 200), but the glucose is almost always normal. CSF myelin basic protein can be elevated.

CT scans show low density in the white matter. The abnormalities are relatively symmetric and are associated with mass effect from the early edema. Changes appear within 18 hours of onset of neurologic symptoms (Rothstein and Shaw 1983). There is sometimes gyral enhancement with contrast, but the white matter does not enhance (Watson et al 1984). Later scans in survivors show hypodensity from demyelination.

MRI is more sensitive than CT. It shows numerous nonenhancing lesions with increased signal intensity in the centrum semiovale and deep white matter, including frontal and temporal lobes and the corpus callosum (Donnet et al 1996; Rosman et al 1997; Friedman 1998). One 23-year-old Belgian woman, 10 days after a measles eruption, had confluent bilateral thalamic and subcortical white matter lesions on MRI (Tshibanda et al 2007). Lesions are hyperintense on T2 MRI, and mixed hypo- and hyper-intense on diffusion-weighted and apparent diffusion coefficient imaging, and they change with time. They are often bilateral but can be asymmetric. Serial MRI shows focal non-hemorrhagic lesions, followed by much larger white matter lesions and later necrosis. Susceptibility-weighted MRI imaging (T2*), which detects paramagnetic blood and iron deposits, shows low-signal large hemorrhages as well as petechial hemorrhages, along with non-displaced medullary veins (Kao et al 2012).
The EEG is abnormal in 90% of these patients. It shows diffuse slowing that may be lateralized.

**Management**

This disease resembles hyperacute experimental allergic encephalomyelitis in animals, a disease ameliorated by glucocorticoids or ACTH. Half of patients treated with high doses of glucocorticoids survive and one sixth of survivors are asymptomatic (Geerts et al 1991). Too-rapid steroid withdrawal may provoke recurrence (Pinto et al 2011).

There are reports of potential benefit of plasmapheresis and intravenous immunoglobulin (Seales and Greer 1991; Kanter et al 1995; Hahn et al 1996; Leake et al 2002). Plasmapheresis is more effective after infections such as mycoplasma pneumonia. Plasma exchange removes antibodies that are likely to participate in the catastrophic damage. Ten exchanges reversed most symptoms in a severe case following mycoplasma pneumonia infection (Ryan et al 2007). Two other cases recovered after plasma exchange plus cyclophosphamide (Seales and Greer 1991; Markus et al 1997), but plasma exchange is not always effective (Ryan et al 2007). In 1 series, aggressive therapy in a neurologic intensive care unit improved prognosis.

The inflammation may have an IL-17 component. The rationales for therapy with type I interferon and anti-IL-17 are presented in the Pathogenesis and pathophysiology section, above.

Two pediatric patients with a partial complement factor I deficiency and this disease did not improve with glucocorticoids and IVIG, but had dramatic resolution with anakinra (anti-IL-1 monoclonal antibody) (Broderick et al 2013).

Hypertonic fluids may reduce CNS edema, but they have no proven benefit. Intracranial pressure monitors help titrate the hyperosmolar agents used to decrease swelling (Mastrodimos et al 1992). Surgical decompression relieves swelling and provides tissue for diagnosis. Before 1990, fewer than half of the patients who were decompressed survived, and all had neurologic sequelae (Geerts et al 1991). At that time, simple supportive care was considered as a treatment option. More recently, 4 patients were treated with high-dose steroids plus decompressive craniotomy. Two recovered completely, and 2 had residual paraplegia without cognitive changes (Taferner et al 2001; Pfausler et al 2002; Ryan et al 2007).

Hypothermia to 33°C reversed many of the manifestations of acute hemorrhagic leukoencephalitis (Takata et al 1999). Hypothermia may affect the blood-brain barrier, cytotoxic edema, or immune function.

**Special considerations**

**Pregnancy**

Pregnancy in relation to acute necrotizing hemorrhagic leukoencephalitis has not been studied.

**Anesthesia**

Anesthesia in relation to acute necrotizing hemorrhagic leukoencephalitis has not been studied.

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**References especially recommended by the author or editor for general reading.

ICD and OMIM codes

ICD codes

ICD-9:
Acute necrotizing hemorrhagic leukoencephalopathy (postinfectious):136.9
Acute necrotizing hemorrhagic leukoencephalopathy (postimmunization or postvaccinal):323.5

ICD-10:
Acute disseminated encephalitis: G04.0
Acute and subacute haemorrhagic leukoencephalitis [Hurst]: G36.1
Subacute necrotizing myelitis: G37.4

Profile

Age range of presentation

0-01 month
01-23 months
02-05 years
06-12 years
13-18 years
19-44 years
45-64 years

Sex preponderance

male>female, >2:1
male>female, >1:1

Family history

none

Heredity

none
Population groups selectively affected

none selectively affected

Occupation groups selectively affected

none selectively affected

Differential diagnosis list

other types of encephalitis
diseases that cause multiple petechial hemorrhages
disease that cause multiple areas of demyelination
acute disseminated encephalomyelitis
acute necrotizing encephalopathy of childhood
multiple sclerosis
bacterial meningitis
brain abscess
epidural empyema
Eastern equine encephalitis
herpes simplex encephalitis
hemorrhagic encephalitis of Baker
Rasmussen encephalitis
brain purpura
pericapillary encephalorrhagia
cerebral venous thrombosis
subarachnoid hemorrhage
acute lead encephalitis
arsphenamine encephalitis
central pontine myelinolysis
reversible toxic spongiform encephalopathy
Reye syndrome
subacute leukoencephalopathy

Associated disorders

Acute disseminated encephalomyelitis
Chickenpox
Chronic nephritis
Hyperacute experimental allergic encephalomyelitis
Measles
Mycoplasmal infection
Tuberculosis
Ulcerative colitis
Upper respiratory tract infection
Viral pneumonia

Other topics to consider

Acute disseminated encephalomyelitis
Progressive multifocal leukoencephalopathy
Transverse myelitis