Journal of Contemporary Neurology

VOLUME 1996, ARTICLE 2
22 MARCH 1996

ISSN 1081-1818. MIT Press Journals, 55 Hayward St., Cambridge, MA 02142, USA; (617) 253-2889; *journals-orders@mit.edu, journals-info@mit.edu*. Published one article at a time in Postscript and PDF source form on the Internet. For more information and other articles see:

- *http://mitpress.mit.edu/jrnls-catalog/cont-neuro.html*
- *gopher.mit.edu*
- anoymous *ftp* at *mitpress.mit.edu*

The MIT Press

Steven C. Cramer, MD[*◆], Alan Segal, MD[*], Ronald Hamilton, MD[+], Jeremy Schmahmann, MD[*], M. Joe Ma, MD[†]

*From the *Department of Neurology and [†]Department of Pathology (Neuropathology), Massachusetts General Hospital, Harvard Medical School; the [+]Division of Neuropathology, Presbyterian University Hospital; and ◆The Clinical Investigator Training Program, Harvard-MIT Division of Health Sciences and Technology in collaboration with Pfizer Inc.*

Leukoencephalitis Due to Varicella Zoster Virus: Report of a Case and Review of Clinical Features

■ This case report describes the clinical features and postmortem diagnosis of varicella zoster virus (VZV) leukoencephalitis in a patient with acquired immunodeficiency syndrome (AIDS) who was taking suppressive doses of acyclovir for a previous disseminated VZV infection. With more patients attaining increased survival in the later stages of AIDS, the incidence of VZV leukoencephalitis will likely rise. Because this is a treatable condition, clinical features of diagnostic value are reviewed. Key features include a history of deep, disseminated, or recurrent VZV infection; rapid progression; very low CD_4 count; and a tendency for hemorrhagic transformation on computed tomography (CT) of the head. The recurrence of VZV infection in a patient taking twice-daily oral acyclovir suggests that an alternate suppressive regimen may be needed after a severe VZV infection in an immunocompromised patient. ■

Key words: VZV, leukoencephalitis, AIDS, hemorrhage, acyclovir

Address correspondence to Steven C. Cramer, MD, Department of Neurology, Bigelow 1256, Massachusetts General Hospital, Fruit Street, Boston, MA 02114.

Address reprint requests to Dr. Cramer.

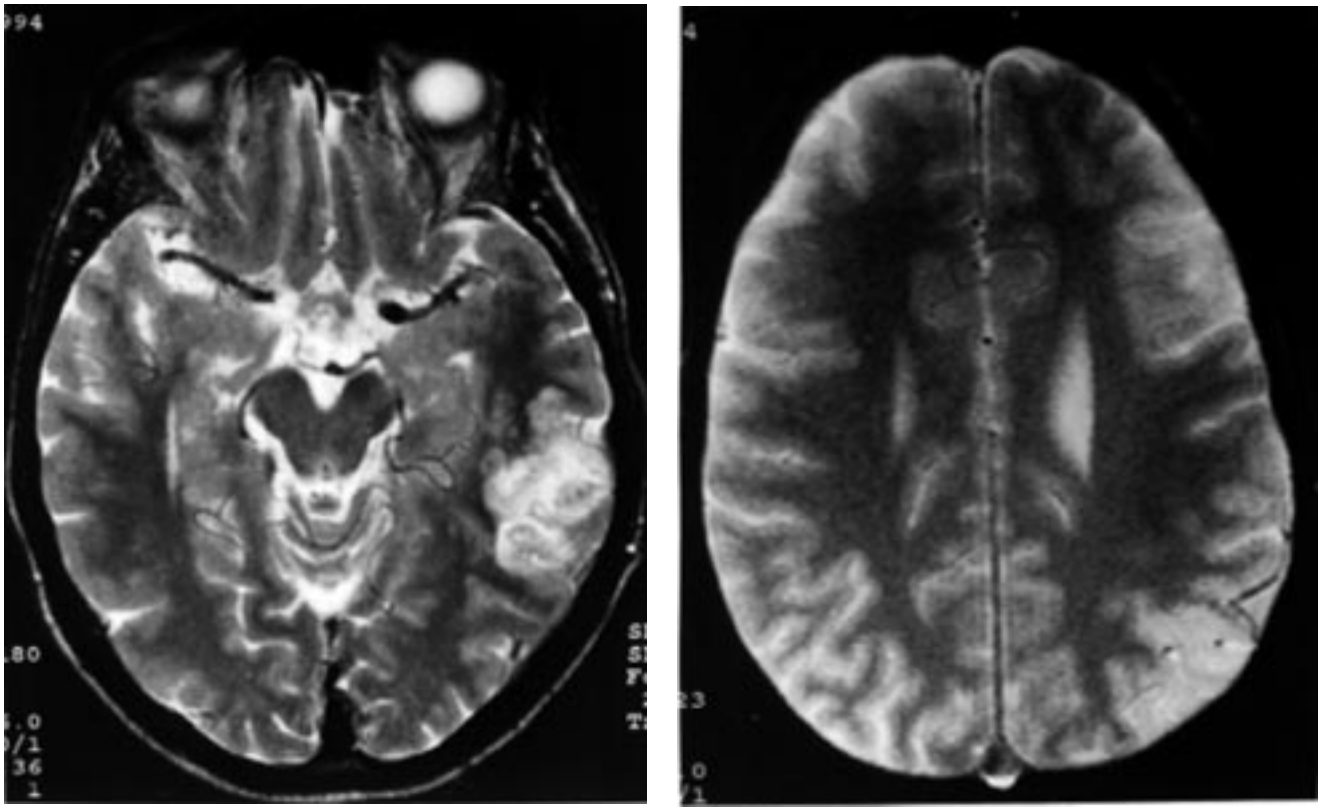
Varicella zoster virus (VZV) has been reported to be an uncommon brain pathogen in AIDS patients, identified in 3 of 153 (2%) (Petito et al, 1986) and 3 of 507 (0.6 %) (Anders et al, 1986) autopsies of the central nervous system (CNS). The incidence of VZV leukoencephalitis may be much higher, however, with previous underestimations due to difficulty of diagnosis (Gray et al, 1994). We review the clinical, radiologic, and pathologic features of a case of VZV leukoencephalitis that developed in a patient with AIDS who was taking suppressive doses of acyclovir twice daily. The diagnostic values of computed tomography (CT), magnetic resonance imaging (MRI), angiogram, lumbar puncture (LP), and brain biopsy are reviewed.

Case Report

The patient was a 37-year-old right-handed man diagnosed with human immunodeficiency virus (HIV) in 1989. His only risk factor was contact with prostitutes. He had a history of *Pneumocystis carinii* pneumonia in 1991. In September 1993, he developed pancreatitis and disseminated vesicular skin lesions; CD4 cell count was 16/μL. Intravenous acyclovir was started for a diagnosis of disseminated VZV. He was discharged on oral acyclovir, 400 mg twice daily, administered by his wife.

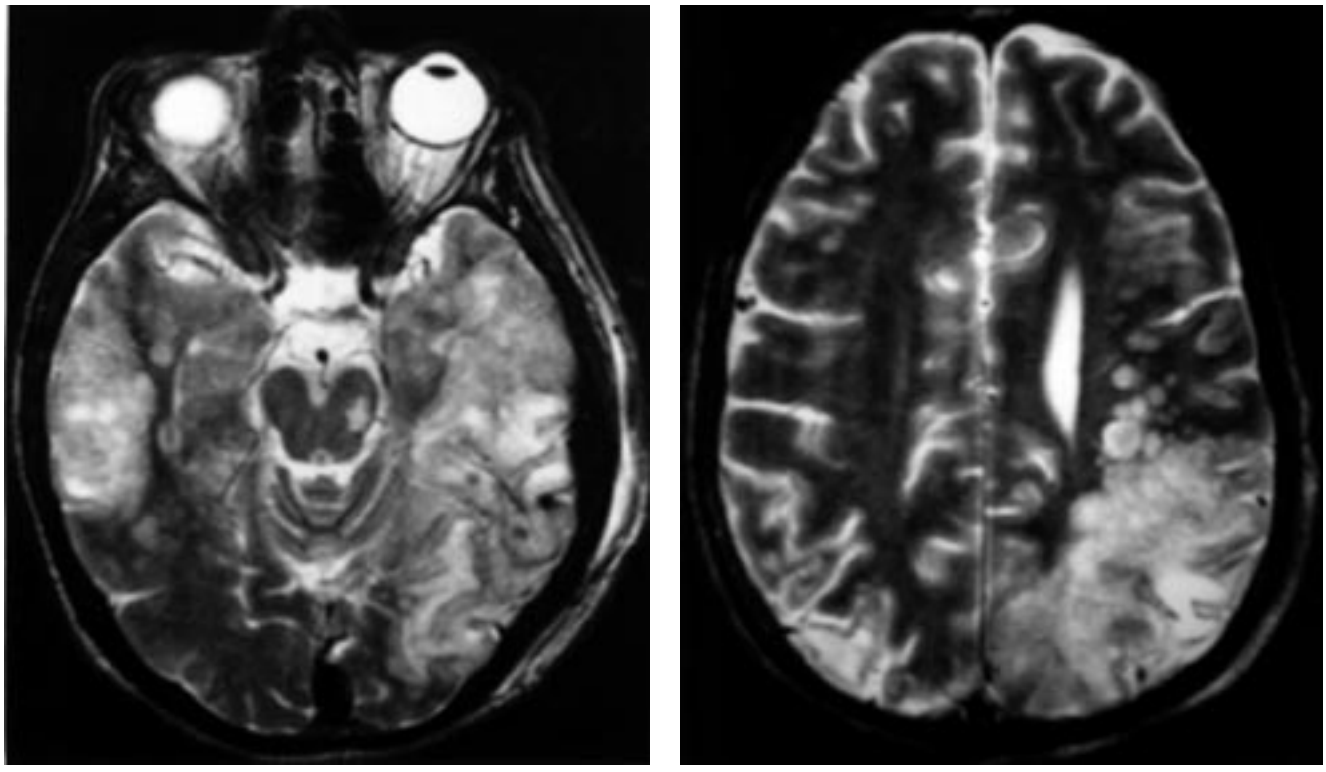
In June 1994 he was found to have a right homonymous hemianopia. An MRI done on June 11 (Fig. 1) showed a left parietal lesion with hemorrhage. Though titers were negative, empiric treatment for toxoplasmosis with oral clindamycin 600 mg three times daily, pyrimethamine 75 mg daily, and leucovorin 10 mg daily was added to his acyclovir.

He was referred to the Massachusetts General Hospital 6 weeks later when he developed increasing confusion. The general physical examination was negative. He was agitated and could perform only one-step commands. He could not differentiate right from left, perform simple calculations, or identify his thumb. His speech was fluent but perseverative. A right visual field defect and decreased right facial sensation were found. Mild right-sided deficits were apparent in sensation and strength. Computed tomography of the head without contrast showed a hemorrhagic lesion in the left posterior temporal lobe which extended to the parietal, occipital, and frontal lobes, associated with extensive edema.



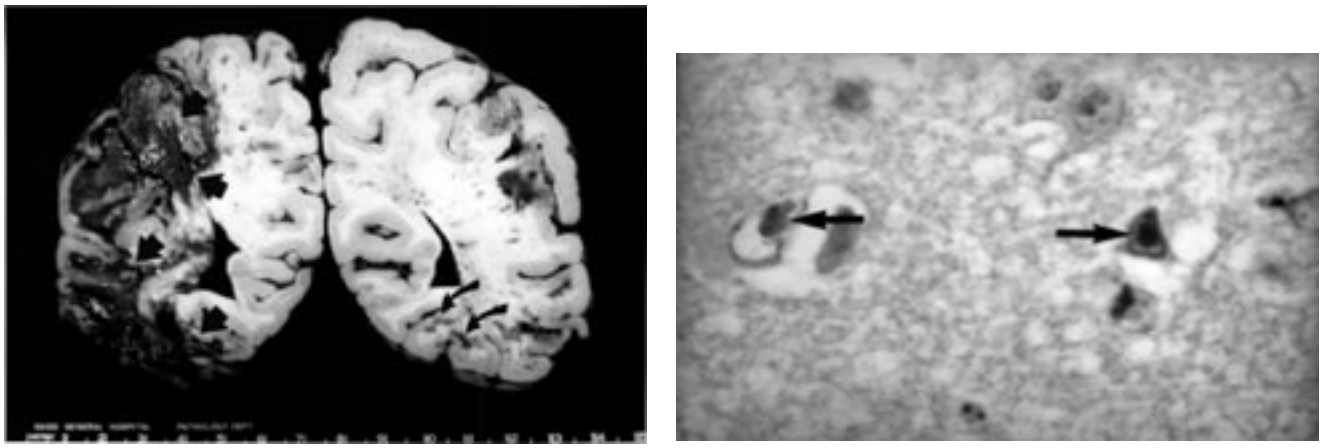
(A) (B)

Figure 1. Magnetic resonance imaging of the brain 11 weeks before death. T2-weighted images demonstrate left parietal lesion with subacute hemorrhage. (A) Level of the midbrain. (B) Top of the lateral ventricles.



(A) (B)

Figure 2. Magnetic resonance imaging of the brain 5 weeks before death. T2-weighted images demonstrate numerous white matter lesions and subacute hemorrhage bilaterally. (A) Level of the midbrain. (B) Top of the lateral ventricles.



(A) (B)

Figure 3. (A) Gross view of a coronal brain section at the parieto-occipital level, showing well-demarcated white matter lesions with necrotic centers (curved arrows). Focal hemorrhage is evident (arrows). (B) Cowdry type A intranuclear inclusions (arrows) found in glial cells (×630).

A small hemorrhagic lesion in the right temporal lobe also was noted. Magnetic resonance imaging with gadolinium (Fig. 2) demonstrated these lesions, as well as one in the left pons, to be T1 hypointense and T2 hyperintense. The left parietal lobe lesion displayed gyral enhancement.

His white blood cell (WBC) count was 2,400/μL with 4% lymphocytes. Extensive hematologic and microbiologic evaluations were otherwise unremarkable. A lumbar puncture showed an opening pressure of 130 mm H_2O, protein of 123 mg/dL, glucose of 60 mg/dL, and no leukocytes. A transthoracic echocardiogram showed no vegetations.

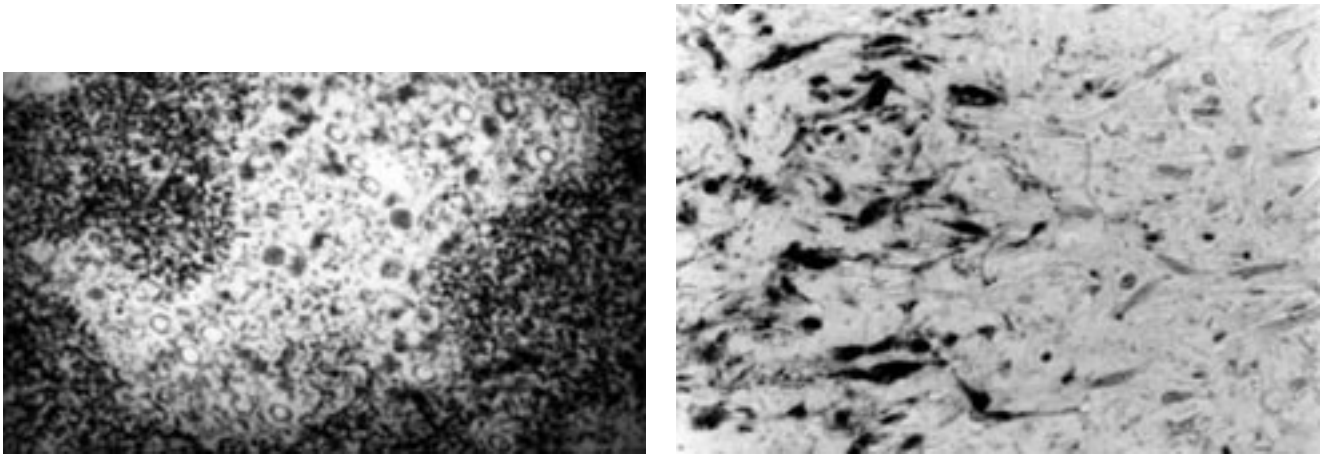
Over the next week the patient showed increasing confusion and could follow no commands. He developed left ptosis and marked right-sided hyperreflexia and extensor plantar response. On day 7 of admission, the patient's WBC count dropped to 1500. Consequently, oral acyclovir and antitoxoplasmosis therapy, continued since admission, were stopped.

On day 11 of admission, open brain biopsy of the large left parietal lesion was performed to identify the cause of a suspected viral leukoencephalopathy. Changes found were consistent only with parenchymal necrosis; cultures and stains for specific microorganisms were negative. The patient became increasingly obtunded. Transfemoral angiography of bilateral carotids arteries, performed on day 21, disclosed only mild narrowing of bilateral supraclinoid internal carotids and proximal anterior cerebral arteries, which were not thought to be supportive of vasculitis. Following discussion with the patient's family, care was withdrawn. He died 34 days after admission.

Permission was obtained for brain autopsy only. The brain weighed 1420 gm. Internal carotids and the major cerebral arteries were remarkable only for minimal atherosclerosis. On brain sectioning, areas of cortical thinning due to underlying white matter lesions were apparent. Multiple, sharply demarcated, round lesions 2 to 10 mm in diameter, and several irregularly shaped, necrotic areas with hemorrhage, were scattered bilaterally in the cerebral white matter and along the cortical gray-white junction (Fig. 3A), as well as in the left optic radiation, putamen, claustrum, and in the midbrain/upper pons. The remainder of the brain and the upper cervical cord were unremarkable.

Most white matter lesions had a target appearance that consisted microscopically of a necrotic center with macrophages and focal hemorrhage surrounded by a paucicellular and edematous periphery of myelin loss rimmed by many reactive astrocytes. Many eosinophilic intranuclear viral inclusion bodies with clear halos (Cowdry type A inclusions) were found in some of the glial cells (Fig. 3B) and cortical neurons. Small blood vessels lined by mitotically active endothelia were present within the lesions, with occasional perivascular cuffs of mononuclear cells. Examination of the major cerebral arteries showed segmental hyperplasia of intimal spindle cells in the proximal left middle cerebral artery, resulting in mild to moderate luminal stenosis, but no viral inclusions, inflammation, or thrombosis. There was no evidence of HIV encephalitis, progressive multifocal leukoencephalitis (PML), or lymphoma.

Ultrastructurally, the viral inclusions contain hexagonal particles characteristic of human herpesviruses (Fig. 4A). Immunohistochemical staining was positive for VZV antigens in these inclusions as well as in some of the hyperplastic intimal spindle cells found in the left middle cerebral artery (Fig. 4B). Stains for toxoplasma organisms, herpes simplex virus types I and II, cytomegalovirus, and HIV were negative. Varicella zoster virus–specific genomic DNA



(A) (B)

Figure 4. (A) Electron microscopic image of hexagonal nucleocapsid particles, measuring 90 to 100 nm in diameter (×89,000). (B) Positive immunostaining for VZV antigens in the hyperplastic spindle cells (bottom half) of thickened vascular intima of left middle cerebral artery (×500). Note that no infiltration by inflammatory cells is present.

was identified in paraffin-embedded tissue taken from a lesion. The methods for immunohistochemistry and DNA analysis have been described previously (Kupperman et al, 1994). Attempts to identify VZV antigens and DNA in biopsy material were unsuccessful due to insufficient quantity of material.

Discussion

Varicella zoster virus infection of the CNS has been reported in more than 4% of patients with AIDS examined at autopsy, but may currently be underdiagnosed (Gray et al, 1994). Varicella zoster virus infection of an immunocompromised patient's CNS can result in a number of different pathologic patterns, including ventriculitis, meningomyeloradiculitis, myelitis, vasculopathy, meningitis, a transsynaptic necrosis, and leukoencephalitis (Gray et al, 1994; Rostad et al, 1989; Poscher 1994). Leukoencephalitis due to VZV has been successfully treated (Carmack et al, 1992; Amlie-Lefond, 1995), making it vital to distinguish this entity from other white matter complications seen in AIDS patients.

Clinical features suggestive of VZV leukoencephalitis include a severely immunocompromised state, rapid progression, a history of severe zoster eruption, and radiologic evidence for a combination of white matter abnormalities, infarct, and hemorrhage (Table 1). Twenty-two immunocompromised cases with clinical correlation were identified from a search of the literature and primary references (Kupperman et al, 1994, 7–16). To be included, patients had to have a multifocal leukoencephalitis and either demonstrate VZV in cerebrospinal fluid (CSF) or brain or show a characteristic appearance on neuropathologic exam. Eight of the cases have been non-AIDS patients and 14, including our case, have been AIDS patients. Eighteen of the patients were male. The median age was 34 years (range, 5 to 69 yr). Among patients with AIDS, VZV leukoencephalitis occurred in the later stages, all reported peripheral blood CD4 values being less than 50/μL.

Neurologic findings in VZV leukoencephalitis included generalized features, such as confusion and coma, as well as focal neurologic abnormalities, including seizure, hemiparesis, aphasia, hemineglect, visual field deficits, ataxia, and brainstem findings. Progression from neurologic presentation to death occurred over a median of 2 months (range, < 1 to 18 mo). A history of zoster eruption was absent in three cases and restricted to a focal dermal eruption in four. In the remaining 15, however, the zoster eruption had been deep, disseminated, or recurrent. Extraneural VZV, when present, preceded leukoencephalitis with a median latency of 3 months (range, 0 to 12 mo).

The presence of CNS hemorrhage in a patient with AIDS is suggestive of VZV leukoencephalitis, because hemorrhage is infrequently seen with other disease processes. Hemorrhage was noted in eight VZV cases and may be the result of vasculopathy or infarct. It has been described uncommonly in a number of conditions such as thrombocytopenia and CNS Kaposi's sarcoma (Levy et al, 1985; Berger et al, 1990), but not with diseases of the white matter (Berger et al, 1987; So et al, 1986; Navia et al, 1986). Central nervous system hemorrhage in the setting of AIDS was noted in none of 113 MRIs of encephalopathic patients (Kupfer et al, 1990) and in one of 154 sequential autopsies (Berger et al, 1990). Hemorrhagic stroke in patients with AIDS is also rare (Engstrom et al, 1989; Mizusawa et al, 1988).

Table 1 Features Helpful in Diagnosis of Varicella Zoster Virus Leukoencephalitis

History
- Immunocompromised state affecting cell-mediated immunity
- Rapid progression over weeks
- History of deep, disseminated, or recurrent zoster eruption
- History of a zoster eruption occurring months prior to CNS process

Radiology
- Intracerebral hemorrhage
- Simultaneous white matter abnormalities and infarct, with or without hemorrhage
- Contrast enhancement of some lesions
- Numerous lesions expanding rapidly

Laboratory
- Peripheral blood CD4 count < 50/μL
- Positive CSF viral culture
- CSF analysis detecting VZV DNA by PCR methods
- Brain biopsy demonstrating VZV by in situ hybridization or immunocytochemistry

Varicella zoster virus leukoencephalitis may present a challenge in diagnosis. These features aid in distinguishing this disease from other white matter processes affecting the brain in AIDS or other immunocompromised states.

In the absence of hemorrhage, radiologic diagnosis of VZV leukoencephalitis is aided by identification of infarct in the setting of white matter abnormalities (Amlie-Lefond et al, 1995; Lentz et al, 1993). Contrast enhancement of lesions is common, unlike PML in which enhancement is uncommon and faint when present (Berger et al, 1987; Lentz et al, 1993; Whiteman et al, 1993). Computed tomography is of limited diagnostic utility for VZV, showing no abnormalities (Gilden et al, 1988; Ryder et al, 1986), subtle subcortical enhancement (Carmack et al, 1992), or enhancing infarct (Kupperman et al, 1994; Amlie-Lefond et al, 1995). Magnetic resonance imaging scanning is more sensitive to the multiplicity and progression of the lesions in VZV leukoencephalitis and may be used to document improvement of lesions with treatment. (Carmack et al, 1992; Lentz et al, 1993).

Angiography in our case showed only minor abnormalities not likely related to the VZV. A transfemoral angiogram was performed in case 2 of the study by Horten et al (1981) and did not show vascular disease. Magnetic resonance angiogram was unremarkable in another case (Amlie-Lefond et al, 1995). Nevertheless, autopsy has shown substantial vascular change in some cases of VZV leukoencephalitis, with leptomeningeal blood vessels exhibiting proliferative changes, severe to total occlusion from thrombosis, or fibrinoid necrosis and frank arteritis with hemorrhage (Amlie-Lefond, 1995; Gray et al, 1992; Morgello et al, 1988). The luminal stenoses seen in our patient at autopsy were poorly depicted on angiogram. Angiogram may therefore be insensitive to the vascular changes accompanying VZV leukoencephalitis.

Routine studies of CSF show elevated protein with fewer than ten leukocytes. This nonspecific formula does not discriminate VZV leukoencephalitis from PML (Berger et al, 1987), lymphoma (So et al, 1986), or toxoplasmosis (Navia et al, 1986), in the setting of AIDS. Levy et al (1985) cultured VZV from the CSF of an AIDS patient diagnosed with encephalitis. Amlie-Lefond et al (1995) recommend diagnosis by polymerase chain reaction (PCR) detection of VZV DNA in CSF, which was performed in one of their cases. Polymerase chain reaction study of CSF has become the most important diagnostic test for herpes simplex virus encephalitis (Tyler 1994) and may be key to improved recognition of VZV leukoencephalitis in the future.

Brain biopsy in our case was nondiagnostic, perhaps relating to choice of biopsy site. Antemortem diagnosis by brain biopsy has been made in two cases by demonstrating VZV using direct fluorescent antibody studies (Carmack et al, 1992) and in situ hybridization (Amlie-Lefond et al, 1995). The hallmark histopathologic changes of VZV leukoencephalitis were seen in our patient at autopsy, consisting of target-like lesions with central necrosis with surrounding myelin degeneration as well as Cowdry A bodies in neurons and glia (Gray et al, 1992). Mild vasculopathy, sometimes seen concomitantly (Gray et al, 1994; Amlie-Lefond et al, 1995), also was present. The Cowdry type A bodies seen on light microscopy and the nucleocapsids seen on electron microscopy are characteristic of herpesviruses. Use of immunocytochemistry, in situ hybridization, or PCR analysis of DNA is necessary, however, to conclusively demonstrate the presence of VZV in brain tissue (Gray et al, 1994).

The optimal regimen for treatment of active VZV leukoencephalitis remains undetermined. Ganciclovir was ineffective in one case (Gray et al, 1992). Carmack et al (1992) achieved sustained improvement using double the recommended dose of intravenous (I.V.) acyclovir (20 mg/kg every 8 hours) in a child with T-cell leukemia; the child was well at 10-month follow-up after completion of treatment. Silliman et al (1993), however, found such doses to be ineffective in one case. Amlie-Lefond et al (1995) used standard doses of IV acyclovir with dexamethasone followed by oral acyclovir, in a patient with advanced AIDS, achieving survival at 5-month follow-up. Improved antemortem diagnosis will allow for further data on treatment of this condition.

A common issue facing the clinician is whether to use suppressive doses of antiviral medication in an immunocompromised patient with zoster eruption to reduce the risk of VZV recurrence. In our case, VZV infection of the CNS developed and progressed despite twice daily doses of 400 mg of acyclovir. Acheson et al (1988) described an AIDS patient in whom a disseminated VZV dermal eruption developed despite acyclovir 400 mg five times daily. Johnston et al (1993) described two AIDS patients who developed presumed VZV retinitis on suppressive doses of oral acyclovir started after a skin eruption; one patient was on 800 mg four times a day, while the other was on 400 mg five times a day. Dellamonica et al (1991) reported two AIDS patients who developed VZV skin lesions on 200-mg oral acyclovir five times daily, but not on 400 mg five times daily. The patient of Amlie-Lefond et al (1995) was alive and recurrence-free after 5 months of oral acyclovir 800 mg three times daily. Herpes zoster eruption occurs commonly in advanced HIV infection, affecting 9% to 13 % of subjects after 2 years (Glesby et al, 1993); further studies are needed to determine the optimal medical regimen to prevent VZV recurrence. Such studies would be particularly important to patients suffering from deep, disseminated, or recurrent VZV episodes, as such features may place them at special risk for recurrence in the CNS.

Increasing survival times in patients with AIDS have been associated with a significant increase in the incidence of several AIDS-related neurologic diseases; this trend is expected to continue (Bacellar et al, 1992). The incidence of VZV leukoencephalitis, a complication of late-stage AIDS, will therefore likely rise. Recognition of characteristic features may permit timely diagnosis and therapeutic intervention.

Acknowledgment

The authors thank Mark Edgar, MD, for his assistance and thoughtful advice.

References

Acheson DWK, Leen CLS, Tariq UZ, Mandal BK. Severe and recurrent varicella-zoster virus infection in a patient with the acquired immune deficiency syndrome. J Infection 1988;16:193–197.

Amlie-Lefond C, Kleinschmidt-DeMasters BK, Mahalingam R, Davis LE, Gilden DH. The vasculopathy of varicella-zoster virus encephalitis. Ann Neurol 1995;37:784–790.

Anders KH, Guerra WF, Tomiyasu U, Verity MA, Vinters HV. The neuropathology of AIDS. UCLA experience and review. Am J Pathol 1986;124:537–558.

Bacellar H, Muñoz A, Miller EN, Cohen BA, Besley D, et al. Temporal trends in the incidence of HIV-1-related neurologic diseases: multicenter AIDS cohort study, 1985–1992. Neurology 1994;44:1892–1900.

Berger JR, Harris JO, Gregorios J, Norenberg M. Cerebrovascular disease in AIDS: a case-control study. AIDS 1990;4:239-244.

Berger JR, Kaszovitz B, Post MJD, Kickinson G. Progressive multifocal leukoencephalopathy associated with human immunodeficiency virus infection. Ann Intern Med 1987;107:78-87.

Carmack MA, Twiss J, Enzmann DR, Amylon MD, Arvin AM. Multifocal leukoencephalitis caused by varicella-zoster virus in a child with leukemia: successful treatment with acyclovir. Pediatr Infect Dis J 1992;12:402–406.

Dellamonica P, Carles M, Lokiec F, Mondain V, Bernard E, Johanson F. Preventing recurrent varicella and herpes zoster with oral acyclovir in HIV-seropositive patients. Clin Pharmacol 1991;10:301–302.

Engstrom JW, Lowenstein DH, Bredesen DE. Cerebral infarctions and transient neurologic deficits associated with acquired immunodeficiency sydnrome. Am J Med 1989;86:528–532.

Gilden DH, Murray RS, Wellish M, Kleinschmidt-DeMasters BK, Vafai A. Chronic progressive varicella-zoster virus encephalitis in an AIDS patient. Neurology 1988;38:1150–1153.

Glesby MJ, Moore RD, Chaisson RE, and the Zidovudine Epidemiology Study Group. Herpes zoster in patients with advanced human immunodeficiency virus infection treated with zidovudine. J Infect Dis 1993;168:1264-1268.

Gray F, Belec L, Lescs MC, et al. Varicella-zoster virus infection of the central nervous system in the acquired immune deficiency syndrome. Brain 1994;117:987-999.

Gray F, Mohr M, Rozenberg F, et al. Varicella-zoster encephalitis in acquired immunodeficiency syndrome: Report of four cases. Neuropathol Appl Neurobiol 1992;18:502–514.

Horten B, Price RW, Jimenez D. Multifocal varicella-zoster virus leukoencephalitis temporally remote from herpes zoster. Ann Neurol 1981;9:251–266.

Johnston WH, Holland GN, Engstrom RE, Rimmer S. Recurrence of presumed varicella-zoster virus retinopathy in patients with acquired immunodeficiency syndrome. Am J Ophthalmol 1993;116:42–50.

Kupfer MC, Zee C-S, Colletti PM, Boswell WD, Rhodes R. MRI evaluation of AIDS-related encephalopathy: toxoplasmosis vs. lymphoma. Mag Reson Imaging 1990;8:51–57.

Kupperman BD, Quiceno JI, Wiley C, et al. Clinical and histopathological study of varicella zoster virus retinitis in patients with acquired immunodeficiency syndrome. Am J Ophthal 1994;118:589–600.

Lentz D, Jordan JE, Pike B, Enzmann DR. MRI in varicella-zoster leukoencephalitis in the immunocompromised host. J Comput Assist Tomogr 1993;17:313–316.

Levy RM, Bredesen DE, Rosenblum ML. Neurological manifestations of the acquired immunodeficiency syndrome (AIDS): experience at UCSF and review of the literature. J Neurosurg 1985;62:475–495.

McCormick WF, Rodnitsky RL. Varicella-zoster encephalomyelitis. Arch Neurol 1969;21:559–570.

Mizusawa H, Hirano A, Shintaku M. Cerebrovascular lesions in acquired immune deficiency syndrome (AIDS). Acta Neuropathol 1988;76:451–457.

Morgello S, Block GA, Price RW, Petito CK. Varicella-zoster virus leukoencephalitis and cerebral vasculopathy. Arch Pathol Lab Med 1988;112:173–177.

Navia BA, Petito CK, Gold JWM, Cho E-S, Jordan BD, Price RW. Cerebral toxoplasmosis complicating the acquired immune deficiency syndrome: clinical and neuropathological findings in 27 patients. Ann Neurol 1986;19:224–238.

Petito CK, Cho E-S, Lemann W, Navia, BA, Price RW. Neuropathology of acquired immunodeficiency syndrome (AIDS): An autopsy review. J Neuropathol Exp Neurol 1986;45:635–646.

Poscher ME. Successful treatment of varicella zoster virus meningoencephalitis in patients with AIDS: Report of four cases and review. AIDS 1994;8:1115–1117.

Rostad SW, Olson K, McDougall J, Shaw C-M, Alvord EC. Transsynaptic spread of varicella zoster virus through the visual system. Hum Pathol 1989;20:174–179.

Ruppenthal M. Changes of the central nervous system in herpes zoster. Acta Neuropathol 1980;52:59–68.

Ryder JW, Croen K, Kleinschmidt-DeMasters BK, Ostrove J, Straus S, Cohn DL. Progressive encephalitis three months after resolution of cutaneous zoster in a patient with AIDS. Ann Neurol 1986;19:182–188.

Silliman CC, Tedder D, Ogle JW, Simon J, Kleinschmidt-DeMasters BK, Manco-Johnson M, Levin MJ. Unsuspected varicella-zoster virus encephalitis in a child with acquired immunodeficiency syndrome. J Pediatr 1993;123:418–422.

So YT, Beckstead JH, Davis RL. Primary central nervous system lymphoma in acquired immune deficiency syndrome: a clinical and pathological study. Ann Neurol 1986;20:566–572.

Tyler KL. Polymerase chain reaction and the diagnosis of viral central nervous system diseases. Ann Neurol 1994;36:809–811.

Whiteman MLH, Post MJD, Berger JR, et al. Progressive multifocal leukoencephalopathy in 47 HIV-seropositive patients: neuroimaging with clinical and pathologic correlation. Radiology 1993;187:233–240.

Journal of Contemporary Neurology is a peer-reviewed and electronically published scholarly journal that covers a broad scope of topics encompassing clinical and basic topics of human neurology, neurosciences and related fields.

Editorial Board