Epstein-Barr Virus Causing Encephalitis in an Elderly Woman

HOWARD EDELSTEIN, MD, and ROBERT T. KNIGHT, MD, Martinez, Calif

INFECTIOUS MONONUCLEOSIS, a common viral infection due to Epstein-Barr virus (EBV), can be associated with diverse neurologic manifestations.1 Encephalitis is unusual but well documented, and has been reported primarily in young patients.2,3 Infectious mononucleosis has recently been described in the elderly, who often have an atypical presentation without the classical triad of pharyngitis, adenopathy, and splenomegaly.4,5 We report a case of encephalitis due to acute EBV infection in an elderly woman who did not have the classical picture of mononucleosis.

CASE REPORT
A 64-year-old white woman had two weeks of fever, rigors, and malaise, without sore throat or cough. Her temperature was 102.9°F (39.4°C), but she had no icterus, pharyngitis, organomegaly, adenopathy, periorbital edema, or petechiae. Significant laboratory values on admission were white blood cell count 2,600/cu mm with 23% segmented neutrophils, 36% band forms, 38% lymphocytes without atypical forms, and 3% monocytes; platelet count 201,000/cu mm; hemoglobin 10.6 gm/dl; hematocrit 31%; SGOT 77 U/L; SGPT 60 U/L; and LDH 842 U/L. A centrifuged specimen of urine obtained by bladder catheterization showed 6 to 10 WBCs per high-power field and numerous bacteria, and culture of urine yielded Escherichia coli. Ureaplasia was tentatively diagnosed and antibiotic therapy was started. Over the next few days the patient defervesced but became confused. A neurologist observed severe lethargy and poor response to verbal commands, but neurologic examination was otherwise unremarkable except for an upward left plantar reflex. Computerized tomography of the head with contrast material was normal; EEG showed mild to moderate generalized slowing as well as intermittent sharp activity in the frontal regions. Lumbar puncture revealed an opening pressure of 210 mm H2O and a closing pressure of 160 mm H2O; CSF values were protein 130 mg/dl; glucose 74 mg/dl; WBC 21/cu mm with 60% lymphocytes, no atypical forms, and 40% monocytes; and RBC 34/cu mm. Isoniazid and rifampin were started as empirical therapy for tuberculous meningitis. A technetium brain scan was normal, and blood and urine cultures were sterile.

By the seventh day the patient became less confused. For the first time lymphocytosis was seen; the peripheral WBC was 8,400/cu mm with 18% segmented neutrophils, 6% band forms, 56% lymphocytes, 12% reactive lymphocytes, 4% monocytes, 1% metamyelocytes, and 1% myelocytes. The SGOT value was 144 U/L, SGPT value 112 U/L, alkaline phosphatase value 407 U/L, and LDH value 1,012 U/L. A PPD was negative, and a CT scan of the abdomen was normal. When a Monospot test was positive, the diagnosis of infectious mononucleosis was considered. Over the next several days lymphocytosis disappeared and confusion and lethargy diminished, but liver enzyme abnormalities persisted. There was no ataxia at this time. A second Monospot test was positive, and serologic findings were consistent with acute EBV infection (Table).

A second CSF specimen on hospital day 11 showed a WBC of 66/cu mm with 92% lymphocytes, 3% neutrophils, and 5% monocytes, an RBC of 30/cu mm, protein value of 148 mg/dl, and glucose value of 71 mg/dl. A large axillary lymph node appeared at this time and persisted through the remainder of the hospital stay. Blood, urine, and stool cultures for virus were negative, as were tests for rheumatoid factor and antinuclear antibody, and an indium-labeled white blood cell scan. Cultures of CSF did not grow mycobacteria, but CSF from the first lumbar puncture grew Aspergillus fumigatus in broth, which was considered to be only a contaminant. The second CSF culture was sterile for bacteria, mycobacteria, and fungi. The patient was discharged on the 19th hospital day with a wide-based gait, difficulty in feeding herself, and mild cognitive impairment. Examination two weeks after discharge showed normal gait and feeding habits and return of liver function parameters to normal ranges. One month after discharge, mentation had returned to normal, and a CBC was normal. She had received no specific antiviral chemotherapy.

DISCUSSION
Infectious mononucleosis is a well recognized disease of teenagers and young adults. By adulthood, 90% to 95% of people have antibodies to EBV.6 In a survey of 3,043 cases of infectious mononucleosis, only 23 (0.76%) occurred in patients more than 40 years old,7 but more recent reports have identified older patients.8,9 Clinical presentation differs between age groups; adenopathy, pharyngitis, and splenomegaly are less common in older patients, whereas jaundice and hepatomegaly are more common.4,5

Neurologic manifestations of infectious mononucleosis include meningitis, optic neuritis, transverse myelitis, Bell’s palsy, polynuertis, Guillain-Barré syndrome, and

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*Tests performed at State Public Health Laboratory, Berkeley, Calif, using standard fluorescent-antibody technique.10

VCA = viral capsid antibody; EA = early antigen; EBNA = EBV-associated nuclear antibody.
encephalitis. The reported frequency of neurologic disease has ranged from 0.37% to 26.5%. Central nervous system involvement may be the sole sign of EBV infection, without other components of the mononucleosis syndrome. As in the patient reported here, the onset of neurologic symptoms occurs most commonly at the peak of clinical illness, usually one to three weeks after the onset of symptoms.

Our patient had cerebellar findings on physical examination, particularly an ataxic gait. Cerebellar abnormalities figure prominently in encephalitis due to EBV and can be a clue to diagnosis of EBV infection in the appropriate situation.

Prognosis for full neurologic recovery from central nervous system EBV infection is generally good, even when the patient exhibits severe impairment, though serious sequelae can persist. In one study, residual neurologic morbidity was estimated at 12% and mortality at less than 8%.

The patient in this report had a firm diagnosis of acute EBV infection on the basis of serologic tests and presence of atypical lymphocytes. EBV infection should therefore be added to the differential diagnosis of encephalitis in adults, including the elderly.

**SUMMARY**

Although infectious mononucleosis commonly afflicts young persons, it is now being described more frequently in the elderly. Neurologic manifestations are uncommon, and encephalitis is rare, especially in elderly patients. We have reported a case of acute Epstein-Barr virus infection causing acute encephalitis in a 64-year-old woman. Despite the severity of encephalitis, the patient recovered fully after several weeks.

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**References**