Can We Predict a Prolonged Course and Intractable Cases of Herpes Simplex Encephalitis?

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In Japan, herpes simplex encephalitis (HSE) has historically been fatal in approximately 30% of all reported cases. After the induction of acyclovir (ACV), however, the mortality rate has decreased to 7.1% (1), and HSE is now regarded as a treatable disease. However, the rate of poor outcome including moderate or severe sequelae still remains at 30-40% of HSE patients, despite standard ACV treatment. It is conceivable that early detection and appropriate treatment will lead to a good prognosis for intractable HSE.

Problems in prolonged and intractable cases of HSE were taken up at the workshop held by the Japan Herpesvirus Infections Forum (JHIF) in 1996 (2) and the symposium of the Japanese Neuro-Infectious Disease Meeting in 1997 (unpublished data). At that time, a tentative definition of intractable cases of HSE was developed as follows:

1. Cases of HSE that develop to an apallic state and to fatality.
2. Prolonged cases that require more than 6 months’ hospitalization.
3. Recurrent cases.

It may be that the main reasons for the development of intractable HSE are a deep consciousness disturbance, status epilepticus, and delays in starting antiviral drug therapy. Conventionally in the USA, a semicoma or coma state in patients over 30 years of age has been accepted as a predictive factor in a fatal prognosis (3).

In this issue of the journal (see also pp 89-94), Taira et al (4) analyzed variable predictors such as age, sex, GCS, initial CT, and cranial computed tomography (CT), as well as magnetic resonance imaging or electroencephalogram abnormalities between the prolonged group (n=8) and non-prolonged group (n=15) in 23 adult HSE patients. The prolonged group was defined as being without any neurological improvement at the time of completion of ACV treatment for 14 days, and they concluded that there are 2 significant predictors of a prolonged course of HSE; a lower GCS ≤ 6 points at the start of antiviral treatment and a higher rate of abnormal lesion on initial CT. The 4 patients of the prolonged group had poor outcomes at 3 months after onset.

The clinical guidelines for adult HSE in Japan recommend a higher dose of ACV for severe HSE patients and alternative therapy of vidarabine in unresponsive cases to ACV treatment (5). A recent study also suggests that corticosteroid administration is a beneficial factor for HSE prognosis (6). Therefore, when HSE patients present with GCS ≤ 6 points and CT abnormal lesion on the temporal lobe, it seems likely that we should initiate ACV treatment at a higher dosage (45-60 mg/day), or add corticosteroid administration including pulse therapy.

However, the pathophysiology for these 2 predictors should be clarified. Intractable cases with a deep consciousness disturbance or wide CT abnormality are often attributed to prolonged herpes simplex virus (HSV) infection or secondary encephalitis (postinfectious/autoimmune encephalitis). Further virologic and immunologic studies are expected to investigate the use of real-time polymerase chain reaction for HSV DNA, and changes of various cytokines in the host response.

References

