Herpes simplex encephalitis is an infrequent infection with high mortality and morbidity. Antiviral therapies decrease mortality but long term sequelae are still high, so early diagnosis is important for opportune treatment. We present a pair of twins with central nervous system herpes simplex infection during the first month of life. Both twins presented non-specific symptoms and consulted with 48 hours apart needing intensive care admission, the first one for noninvasive mechanical ventilation and the second for hemodynamic support. Diagnosis was made by cerebrospinal fluid PCR, in the first twin at day 9 of disease and in the second at admission. Both twins were treated with acyclovir, but only the second one at the beginning of her illness. Initial study with electroencephalogram and magnetic resonance was normal and cerebrospinal fluid on day 18 of treatment was negative for herpes simplex virus DNA detection in both patients.