Herpes Simplex Encephalitis with Intracerebral Hemorrhage

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Herpes simplex encephalitis (HSE) is an important cause of morbidity and mortality. It is caused by Herpes Simplex Virus 1. Intracerebral haemorrhage (ICH) is infrequent complication of HSE. Non improvement in HSE patients can be due to ICH. We report a patient with HSE who developed ICH and was managed conservatively. Herpes simplex encephalitis (HSE) is caused by HSV1 virus. It is non epidemic encephalitis that can be associated with high morbidity and mortality if not treated timely. Up to 2.5 cases per million population per year of HSE are reported.\(^1\) Mortality in untreated HSE patients is about 70%.\(^1\) Some form of cerebral dysfunction is noted in 44-86% of HSE patients after recovery.\(^1,2\) HSE cause necro-inflammation that may cause haemorrhages which are generally small. Large intra-cerebral haemorrhages (ICH) however occur infrequently in HSE.\(^3\) We report a young patient with HSE who developed ICH.

Case Report

A 19 year old Asian male with no previously known pre-morbid illnesses, presented with headache, fever, and fits. Headache was left sided and was there for last seven days. High grade fever with chills, increased irritability, and fits followed, it and were present for last 4 days before presentation. Fits were generalized tonic clonic associated with tongue bite and urinary incontinence. Altered level of consciousness followed fits. Prior to onset of illness there was no history of head trauma, vomiting, vision changes or fits. His pulse was 110/minute, blood pressure 110/70 mm of Hg, respiratory rate 16/minute and temperature 102°F. He was drowsy, irritable and was not following commands, but responded by localizing painful stimulus. Glasgow Coma Score(GCS) was 9/15 (E\(^2\)V\(^2\)M\(^5\)). Pupils were round, regular and reactive to light. Signs of meningeal irritation were negative. Plantar responses were bilaterally extensor. Upper motor neuron type right facial palsy was present. Power was 4/5 in all four limbs and deep tendon reflexes were bilaterally +2. Fundus examination revealed no abnormality. Rest of the systemic examination was unremarkable.

His complete blood picture showed, hemoglobin 14g%, total leukocyte count of 11.5 x 10\(^9\)/L with 83.8% neutrophils, and platelet count 113x10\(^9\)/L. Erythrocyte sedimentation rate was 65. Complete biochemical profile was unremarkable. Coagulation profile and bleeding time were normal. Peripheral blood smear for malarial parasite was negative. Cerebro-spinal fluid (CSF) routine examination showed clear fluid with no xanthochromia, lymphocytes30/mm\(^3\), protein 36 mg/dl, and glucose more than half of serum glucose noted at time of lumbar puncture. No atypical, malignant cells or organism were noted on Gram and Ziehl–Nelsen staining of CSF. Plain CT scan brain showed small hemorrhagic infarct in right temporal parenchyma (Figure 1). Abnormal T2/FLAIR bright signal in the left temporal and posterior basi-frontal lobe with gyriform hyperintense signal on T1 sequence suggestive of hemorrhagic herpes encephalitis were noted on the subsequently performed MRI (Figure 2, 3, and 4). At admission patient was treated with intravenous acyclovir 500mg thrice daily, intravenous ceftriaxone 1g twice daily, dexamethasone 4mg every 4 hourly, and 1g loading dose of valproic acid followed by 500 mg thrice daily. 24 hours after starting treatment, patient’s conscious level improved and no further seizures were observed. GCS improved to 12/15 (E\(^4\)V\(^2\)M\(^6\)). Bilateral flexor plantar response was noted at that time as well. On fifth post admission day the CSF polymerase chain reaction for HSV1 DNA returned positive. On the day of discharge patient had regained full consciousness, was oriented in person, place and time but facial muscle weakness and motor dysphasia persisted. On follow up some learning
disability was observed as patient’s Mini Mental State Examination (MMSE) score was 23/30. Minimal facial muscle weakness persisted. His speech was slow and slurred, but comprehensible.

Fig. 2 Abnormal signal in left temporal lobe on DWI sequence

Fig. 3 Abnormal T2/Flare signal in the left temporal and posterior basifrontal lobe with gyriform hyperintense signal on T1 sequence suggestive of hemorrhagic herpes encephalitis

Fig. 4 Lateral view showing hemorrhagic focus in post contrast MRI Brain.

Discussion
Pathogenesis of HSV encephalitis involves both direct i.e., virus mediated and indirect i.e., immune mediated damage. Intra cerebral ischemic infarcts, vasculopathies and persistent neurological deficit are complications associated with HSV encephalitis. ICH, and issues related with acyclovir are suspected in settings of HSVE when; 1) patient doesn’t improve, 2) clinical deterioration occurs, and 3) focal neurological signs develop. Acyclovir related issues include resistance and side effects. Brain imaging is the best way to evaluate acyclovir unrelated complications. It should be therefore done in all patients who are not improving. Decompressive neurosurgical intervention is required if HSE patients with ICH are not improving or clinical deterioration occurs. Necrotizing granulomatous arteritis, chronic vasculitis, thrombosis of cerebral vessels and ICH can complicate HSV related vasculopathy. Haemorrhagic transformation in HSV encephalitis is considered to be due to two main reasons. Small vessel vasculitis lead to bleeding according to one theory. According to other it primarily viral related brain damage that leads to increased susceptibility to bleeding. Patients with HSVE and ICH generally seek medical advice earlier in the course of illness. Most of patients sought medical advice on first day of illness. Our patient comparatively was brought to hospital late. ICH usually occurs late in course of HSVE. In one study it was noted on 10 or more days after onset of symptoms in 65% patients. Our patient was noted to have ICH earlier.

References