

## Intracerebral hemorrhages as an atypical radiographic presentation of herpes simplex encephalitis on CT scan: An analysis of 23 patients

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### ABSTRACT

**Objectives:** To find out the effect of the atypical presentation of herpes encephalitis in the form of intracerebral Hemorrhage on the morbidity and mortality of patients

**Methodology:** It is basically retrospective study conducted at radiology department Dow University of Health Sciences Civil Hospital, Karachi from 2009 to 2011. Total numbers of patients presented with clinical diagnosis of encephalitis were 109 and underwent CT scan plain and post contrast study. Physical diagnosis was based on fever, fits and altered level of consciousness. Laboratory diagnosis was based on pleocytosis with predominant lymphocytes, low glucose and high proteins and confirmation by polymerase chain reaction test (PCR) and empirical use of acyclovir.

**Results:** Total cases presented with clinical diagnosis of viral encephalitis and presented as hypo density with focal edema on CT scan were 109, out of which 23 cases presented with intracerebral hemorrhages. Hemorrhagic encephalitis was found in 21% of the cases. On plain CT scan brain, five cases showed isolated bilateral basal ganglia and thalamic hemorrhages. In seven cases bilateral temporofrontal region showed hemorrhages. Nine cases showed unilateral temporoparietal region (six cases were on right side and three cases were on left side) hemorrhages and in three cases unilateral right frontoparietal and basal ganglia hemorrhages were found on CT scan. In five cases leptomeningeal enhancement was associated with bilateral temporoparietal encephalitis. Hemorrhage size ranged from 2-5 cm. In nineteen cases, post contrast enhancement was seen in areas of encephalitis.

**Conclusion:** In appropriate clinical setting of encephalitis with CT SCAN diagnosis of intracerebral unilateral or bilateral hemorrhages and post contrast enhancement with CSF positive criteria for viral infection, diagnosis of herpes encephalitis should be on top of differential diagnosis. An early use of acyclovir without waiting for further tests can save the life of patients and significantly reduce the mortality and morbidity of patients.

**KEY WORDS:** Polymerase chain reaction, Herpes simplex encephalitis, Herpes simplex virus, Japanese encephalitis, Computerized tomography angiography, Intracerebral hemorrhage.

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### INTRODUCTION

Herpes simplex encephalitis is a treatable disease; however, untreated infections may progress to coma and death in about 75% cases<sup>1</sup> hence high degree of suspicion and early diagnosis are mandatory. However, atypical presentations may be a cause of

delay in diagnosis and treatment and hence may lead to high morbidity and mortality.

Viral infections are the most important cause of encephalitis. There are over 100 viruses that can result in encephalitis. The patients usually presents with fever and varying degree of alteration in sensorium, which may be associated with focal neurological signs or seizures. In such patients, malaria, bacterial meningitis and non infectious causes of encephalopathy must carefully be excluded. Viral encephalitis generally results in nonspecific clinical picture with some specific features of anatomical involvement such as behavioral changes, aphasia or partial complex seizure in herpes simplex encephalitis (HSE) because of characteristic frontotemporal involvement.

There are estimates that HSE is the most important cause of treatable viral encephalitis with an incidence of 1 case/million population/year. Certain viruses are prevalent in certain regions. Japanese encephalitis (JE) in South East Asia, West Nile encephalitis is Middle East, St. Luis encephalitis and equine encephalitis in America. The incidence of clinically diagnosable encephalitis is between 3.5-7.4/100,000 population/year; however in children the incidence is much higher.<sup>2,3</sup> Intracerebral hemorrhage is considered rare in herpes encephalitis and few cases are published as case reports in international literature.<sup>4-6</sup>

Our objective was to find out the effect of the atypical presentation of herpes encephalitis in form of intracerebral Hemorrhage on the morbidity and mortality of patients.

## METHODOLOGY

It is basically retrospective study conducted at Radiology Department from 2009 to 2011. Total numbers of patients who presented with clinical diagnosis of encephalitis were 109 and underwent CT scan plain and post contrast study. Twenty three cases showed intracerebral unilateral or bilateral hemorrhages on CT scan. These twenty three cases were selected for study because intracerebral hemorrhage is considered rare in herpes encephalitis in international literature and despite clinical picture of encephalitis clinician try to exclude other causes of intracerebral hemorrhage and wait for PCR to confirm diagnosis of herpes encephalitis. Clinical diagnosis was based on fever, fits and altered level of consciousness.

Laboratory diagnosis was based on pleocytosis with predominant lymphocytes, low glucose and high proteins and confirmation by polymerase

chain reaction test (PCR) which was done in twelve cases only due to financial constraints. In twelve patients acyclovir was given within 5-6 hours of sign and symptoms on empirical basis as patients were not affording while in eight patients waited for PCR. In three cases while PCR test was awaited, in the mean time acyclovir was given empirically at 48 hours of admission because of rapid deterioration clinically. Rest of patients received acyclovir post PCR result after five days.

CTA, Routine blood examination including Hb, total count and differential count, ESR, Blood Biochemistry including, sugar, urea, creatinine and LFT and serum for ANF, Blood coagulation profile, ECG and ECHO-cardiography, and USG of abdomen were normal, which along with clinical scenario excluded the other causes of intracerebral hemorrhages.

**Inclusion criteria:** Cases which presented with intracerebral hemorrhages, along with clinical suspicious of encephalitis.

**Exclusion criteria:** (1) Cases without intracerebral hemorrhages with clinical suspicious of encephalitis. (2) Other causes of intracranial hemorrhages such as trauma, other causes of viral encephalitis, hypertension, coagulopathy, vasculitis etc.

## RESULTS

Total number of patients presented with clinical diagnosis and CSF D/R based diagnosis of herpes encephalitis were 109 and underwent CT scan both plain and post contrast study. Total numbers of patients presented with intracerebral focal edema with hemorrhages were twenty three, in which nine were children and fourteen adults and these patients were selected for this study. Patients presented with low grade fever, headache for 3-5 days and fits of tonic clonic nature 5-10 hours prior to admission. Temperature ranged from 37.5 to 39 degree centigrade (37.5 -39 C). Signs of meningism were seen in five patients.

Clinical presentation was an acute febrile illness associated with behavioral abnormalities, altered sensorium, abnormal movements, and focal neurodeficits in various combinations. CSF showed slight increased protein, normal glucose levels, and mild pleocytosis with predominantly lymphocytes. PCR was positive for HSV in nine cases. In three cases PCR test was negative. On plain CT scan brain, five cases showed isolated bilateral basal ganglia and thalamic hemorrhages. In seven cases, bilateral temporofrontal region showed hemorrhages, while nine cases showed unilateral temporoparietal

region (six cases on right side and three cases on left side). In three cases unilateral right frontoparietal and basal ganglia hemorrhages were documented. In five cases leptomeningeal enhancement was associated with bilateral temporoparietal encephalitis. Hemorrhage size ranged from 2-5cm.

Nineteen cases showed post contrast enhancement in areas of encephalitis. In eight cases clinician waited for PCR results and then started acyclovir therapy. In five cases no response was seen and patient died while in three cases significant morbidity was seen either with movement disorder, fits, and focal neurological deficits or in combinations. In fifteen cases acyclovir was given at early stage and responded promptly without residual post encephalitis sequelae. In eight patients, acyclovir was given after PCR test.

## DISCUSSION

Herpes simplex encephalitis is the commonest type of encephalitis seen in patients both in children and adults and it is treatable disease but if remain untreated or delayed in diagnosis, leads to high morbidity and mortality.<sup>1</sup> Hence high degree of suspicion and early diagnosis are mandatory. However, atypical presentation may be a cause of delay in diagnosis and treatment and hence may lead to high morbidity and mortality. Many viral forms of encephalitis involve the thalami and basal ganglia including West Nile encephalitis, Japanese encephalitis, Murray Valley encephalitis, Eastern equine encephalitis, and rabies<sup>7-11</sup> but it is documented in many articles that bilateral basal ganglia and thalami involvement are rarely seen in herpes simplex encephalitis presented with fits.<sup>12-17</sup>

It is also claimed that even more rarely bilateral hemorrhagic lesions in basal ganglia and thalami are seen in herpes simplex encephalitis and commonly seen in Japanese and other viral encephalitis.<sup>18</sup> In this study, 5 cases showed isolated involvement of bilateral basal ganglia and thalamic hemorrhages. These cases proved to be HSE in nature and responded promptly to intravenous acyclovir. Due to atypical presentations diagnosis was delayed and usually physicians waited for PCR test as result required 4-5 days to come. As serological report may be delayed, early radiological evidence is very much helpful for suspecting Herpes encephalitis, especially in a setting of atypical presentations<sup>18</sup>. Even in cases of HSV, it is not necessary that PCR is found to be positive.<sup>12</sup>

In many studies it is documented that hemorrhages are rarely associated with herpes encephalitis and

it is very unusual presentation. The hemorrhagic herpes encephalitis has documented as case report because of rarity in many articles.<sup>19-23</sup> In one large study, not a single case showed hemorrhage in all cases of herpes encephalitis.<sup>24</sup> While in this study 23 cases (21%) are associated with large hemorrhages of 2-5 cm which are rare in literature, so in presence of hemorrhage on CT scan with appropriate clinical scenario of encephalitis along with CSF positive criteria for viral infection, herpes encephalitis should be on top of list of differential diagnosis and early acyclovir therapy should be started without delay and waiting for PCR.

In this study 15 patients promptly responded to acyclovir because of early therapy while five patients died and three patients showed neurological deficits and behavioral problems as well as fits because of delayed management. JE is a severe form of endemic flavivirus encephalitis manifesting with features of encephalitis or encephalomyelitis. In a study on radiological changes in JE, CT scan was done in 38 and MRI in 31 patients. Thalamic involvement was present in 93.5%, basal ganglia in 35%, mid brain in 58%, Pons in 26% and cerebral cortex in 19.4% of patients.<sup>25</sup>

Similar findings have been reported in earlier autopsy studies.<sup>26-28</sup> Herpes encephalitis closely mimics with Japanese encephalitis clinically and radiologically if patients present with intracranial hemorrhages and the fact that Japanese encephalitis is managed conservatively so acyclovir should be given empirically without waiting for further tests in order to avoid delay in patient management. In all those cases where early acyclovir was given, response was prompt, patients recovered fully without any significant comorbidities hence no mortality or morbidity was noted in 15 cases while in eight cases where diagnosis was delayed and waited for test such as PCR then acyclovir was started, in these cases, five died and three showed significant morbidity. Size, location, multiplicity, unilateral or bilateral distribution of intracranial hemorrhage did not show any impact on morbidity or mortality of patients.

## CONCLUSION

In appropriate clinical setting of encephalitis with CT SCAN diagnosis of intracerebral unilateral or bilateral hemorrhages and post contrast enhancement with CSF positive criteria for viral infection, diagnosis of herpes encephalitis should be on top of differential diagnosis. With early use of acyclovir without waiting for further tests,

patient's lives can be saved and hence mortality and morbidity of patients can be reduced significantly. Closest differential diagnosis is that of Japanese encephalitis which is managed conservatively while other differential diagnosis can be ruled out by appropriate clinical scenario and commonly available cheap tests.

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