Case report

Epileptic Disord 2006; 8 (1): 57-60

Herpes encephalitis as a cause of nonconvulsive status epilepticus

Aysegul Gunduz[1], Ali Fuat Beskardes[2], Ayse Kutlu[1], Cigdem Ozkara[1], Naci Karaagac[1], Seher Naz Yeni[1]

[1] IU. Cerrahpasa Medical Faculty, Department of Neurology
[2] Department of Psychiatry, Istanbul, Turkey

Received July 27, 2005; Accepted January 20, 2006

ABSTRACT – Nonconvulsive status epilepticus is a specific form of status epilepticus characterized by alteration in mental status and persistent seizure activity on EEG, with or without motor phenomena. Recognition of the consequences of nonconvulsive status epilepticus has attracted greater attention to this condition. We present a 24-year-old woman with epilepsy who developed nonconvulsive status epilepticus during pregnancy. Despite treatment with antiepileptic drugs, the seizures persisted and confusion deepened. Further workup to explain the etiology revealed the diagnosis as herpes encephalitis. She recovered completely by the third day of parenteral acyclovir administration. *Herpes simplex* encephalitis causing nonconvulsive status epilepticus in a pregnant, epileptic woman is an unfortunate and unusual condition, which was simultaneously complicated by the presence of multiple etiological factors.

Key words: nonconvulsive status epilepticus, *Herpes* encephalitis, pregnancy, epilepsy

Nonconvulsive status epilepticus (NCSE) is a form of status epilepticus (SE) characterized by alteration in mental status and persistent focal or generalised seizure activity on EEG. NCSE is estimated to have an incidence of 1.5/100 000, and accounts for up to 20% of all SE cases (Celesia 1976, Tomson *et al*. 1992). NCSE is classified according to age or seizure type as absence SE, simple partial SE, complex partial SE or myoclonic SE (Walker *et al*. 2005). However, there are clinical overlaps. It has gained interest due to its wide spectrum of clinical presentation, which causes diagnostic difficulties. Among its various causes, epileptic syndromes, metabolic disturbances such as renal insufficiency, and hyponatremia, anoxic/hypoxic brain insults, alcohol, antiepileptic drug (AED) and antibiotic use, withdrawal from alcohol or AED, cerebrovascular accident, head trauma or tumor are attracting attention (Chedrawi *et al*. 2004, Tomson *et al*. 1992, Towne *et al*. 2000, Walker *et al*. 2005). Infectious diseases, such as AIDS with cerebral cryptoccocus, are also reported to be among the causes of NCSE (Cury *et al*. 2004). However, although *Herpes simplex* virus (HSV) is the most common cause of acute encephalitis and a frequent cause of seizures in encephalitis, to our knowledge NCSE has not been previously reported in *Herpes simplex* encephalitis (HSE).

HSE is characterised by subacute progression of fever, headache, altered level of consciousness, presence of olfactory hallucinations, focal neuro-

Correspondence:
A. Gunduz
Cerrahpasa Medical Faculty,
34098 K.M.Pasa/Istanbul,
Turkey
Tel.: +00 90 212 41 43000/21078,
212 63 30176;
fax: +00 90 212 63 30176.
<draysegulgunduz@yahoo.com>

logical deficits, CSF pleocytosis and abnormal neuroimaging findings (Roos 2005). Seizures in HSE may be focal or generalised. Focal motor seizures are a common, presenting sign, especially in children (Lahat *et al*. 1999). Atypical cases of *Herpes* encephalitis with lack of focal features, abnormal CSF and MRI findings have also been reported in up to 20% of cases (Fodor *et al*. 1998).

In this case report, we present an epileptic patient who developed resistant NCSE and secondarily generalised seizures due to *Herpes* encephalitis, during pregnancy.

Case report

A 24-year-old woman, at seven weeks' gestation, was admitted to our clinic with complaints of headache and stagnation. Her headache had started three days prior to admittance, and had gradually increased in severity. On the second day of headache, her family noticed an impairment of awareness and episodes of unresponsiveness. She had been followed for ten years for cryptogenic partial epilepsy by one of the staff neurologists (SNY). She had had daily complex partial seizures (CPS) resembling current episodes and nocturnal secondarily generalised tonic-clonic (SGTC) seizures. She was in remission under 800 mg/day carbamazepine apart from a single SGTC seizure three years earlier due to AED withdrawal during her first pregnancy.

Previous interictal EEG showed right temporal slow waves and cranial MRI was normal. Her family history revealed partial epilepsy in her sister with a benign course.

On admission, she presented a low grade fever. At times she became unresponsive, interruption of communication was observed, and she had bilateral, unresponsive plantar reflexes. The rest of the neurological examination was normal.

All laboratory investigations including complete blood count, extensive biochemistry, thyroid hormone levels and urinalysis were within normal ranges except for mild leukocytosis, and slight increases in ESR and CRP levels. The carbamazepine blood level was within the theurapeutic range (7.9 mic/mL). Initial EEG revealed frequent episodes of incremental rhythms, and spike and wave patterns prominent over right fronto-temporal leads lasting for 60-200 seconds *(figure 1)*. When she was asked to count during the EEG recording, she stopped counting and became unresponsive during the ictal episodes. The EEG was normal between the episodes. Carbamazepine was increased to 1,600 mg/day. Despite treatment with iv diazepam and phenytoin on subsequent days, the seizures persisted and confusion deepened. The EEG recorded on the second day of her admission showed more frequent and diffuse ictal patterns. On the third day of admission, she had partial seizures that started from the unilateral face spreading to the corresponding side of the body; she then developed SGTC seizures while ictal activity on the EEG became more aggravated *(figure 2)*. As the persistence of

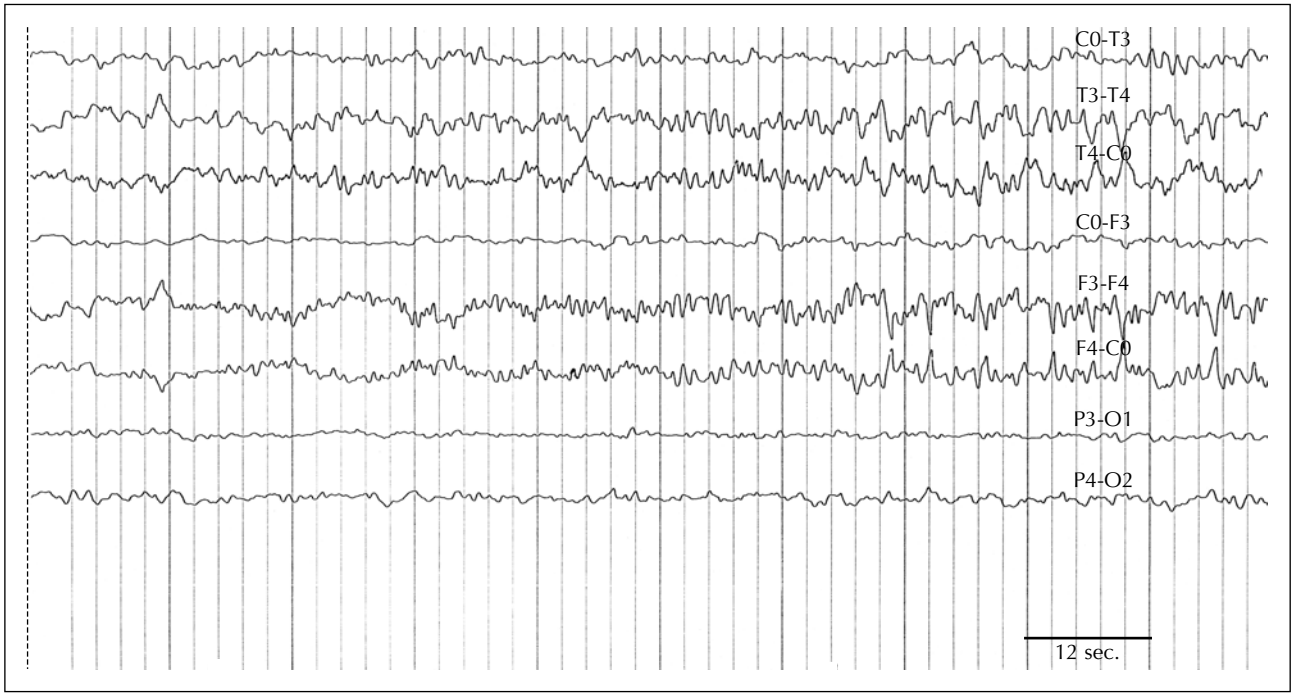

Figure 1. Initial EEG revealed frequent episodes of spike wave patterns prominent over right frontotemporal leads lasting 60-200 seconds.

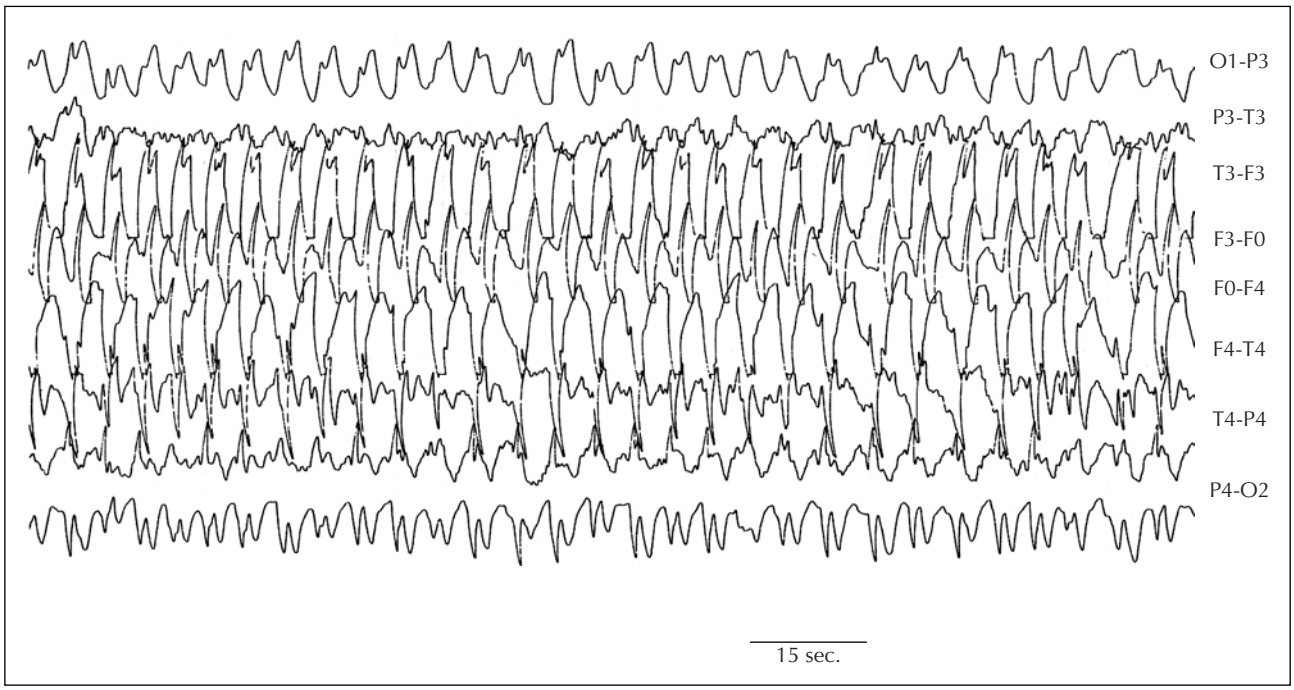

Figure 2. Ictal patterns became more prominent and persistent on third day EEG.

NCSE raised the suspicion of other etiological factors including encephalitis, further workup was performed to rule out etiological factors other than pregnancy and history of epilepsy. Although cranial MRI with gadolinium and biochemical and cellular analysis of cerebrospinal fluid (CSF) were normal, empiric therapy with acyclovir (30 mg/kg/day) was instituted while waiting for HSV DNA detection by PCR. Her convulsive and nonconvulsive seizures stopped after the antiviral therapy and she recovered completely by the third day of treatment. HSV DNA PCR in the CSF was later reported to be positive, confirming the diagnosis. Her pregnancy was also terminated. As regards follow-up, she has had no seizure relapse on 600 mg/day carbamazepine, for ten months.

Discussion

We present an epileptic patient who developed NCSE during pregnancy. Several factors may cause this type of SE, one of which is pregnancy in a patient with epilepsy. Seizures may increase in a third to a quarter of patients during pregnancy for several reasons, including decreased levels of circulating, unbound AEDs, increase in metabolism of AEDs and volume of distribution, poor absorption from the gastrointestinal tract, hormonal changes, sleep deprivation, emotional factors, mild respiratory alkalosis and AED non-compliance (Yerby and El-Sayed 2003).

Comorbidity with metabolic disorders such as uremia, the use of antibiotics, or the presence of infections can also trigger NCSE (Chedrawi *et al*. 2004). Generally, NCSE in epileptic patients has been demonstrated to have a better prognosis than NCSE with acute symptomatic events (Shneker and Fountain 2003).

In our patient, the inability to control seizures, the worsening of headache, and deepening of confusion, despite the appropriate AED treatment, necessitated further investigation. Although cranial MRI and biochemical analysis of CSF were within normal ranges, acyclovir treatment was started, in the knowledge that 5.8% of cases of HSE may have normal CSF and 10% normal imaging results (Tyler 2004). The dramatic response to treatment, as well as the CSF proving positive for HSV DNA confirmed our diagnosis. CSF PCR has a sensitivity of 98% and specificity of up to 100% (Aurelius *et al*. 1991).

Our patient's case was complicated by the presence of multiple factors, which may have triggered the seizures and the convulsive status epilepticus. HSV has a tendency to attack temporal lobes via the olfactory pathways. Clinical and electrophysiological evidence for the seizures arising from fronto-temporal regions in our patient was another clue to the diagnosis of HSE because focal seizures as the presenting sign is known for HSE in children. This was an interesting and challenging case, as the HSE might have either created a *de novo* epileptogenic zone or precipitated her habitual, but apparently benign seizures, giving rise to NCSE with the probable, predisposing effect of pregnancy.

This is the first case report of NCSE induced by HSE during pregnancy in a woman with epilepsy. This highlights the possibility of multiple risk factors. We also would like to

emphasize the importance of extended workup to ensure a favourable outcome in patients with NCSE. □

References

Aurelius E, Johansson B, Sköldenberg B, Staland A, Forsgren M. Rapid diagnosis of herpes simplex encephalitis by nested polymerase chain reaction assay of cerebrospinal fluid. *Lancet* 1991; 337: 189-92.

Celesia GG. Modern concepts of status epilepticus. *JAMA* 1976; 235: 1571-4.

Chedrawi AK, Gharaybeh SI, Al-Ghwery SA, Al-Mohaimeed SA, Alshahwan SA. Cephalosporin-induced nonconvulsive status epilepticus in a uremic child. *Pediatr Neurol* 2004; 30: 135-9.

Cury RF, Wichert-Ana L, Sakamoto AC, Fernandes RM. Focal nonconvulsive status epilepticus associated to PLEDs and intense focal hyperemia in an AIDS patient. *Seizure* 2004; 13: 358-61.

Fodor PA, Levin MJ, Weinberg A, Sandberg E, Sylman J, Tyler KL. Atypical herpes simplex virus encephalitis diagnosed by PCR amplification of viral DNA from CSF. *Neurology* 1998; 51: 554-9.

Lahat E, Barr J, Barkai G, Paret G, Brand N, Barzilai A. Long term neurological outcome of herpes encephalitis. *Arch Dis Child* 1999; 80: 69-71.

Roos KL. Encephalitis. In: *Roos KL. Principles of neurologic infectious diseases.* USA: The McGraw-Hill, 2005: 65-76.

Shneker BF, Fountain NB. Assessment of acute morbidity and nonconvulsive status epilepticus. *Neurology* 2003; 61: 1066-73.

Tomson T, Lindbom U, Nilsson BY. Nonconvulsive status epilepticus in adults: thirty-two consecutive patients from a general hospital population. *Epilepsia* 1992; 33: 829-35.

Towne AR, Waterhouse EJ, Boggs JG, *et al.* Prevalence of nonconvulsive status epilepticus in comatose patients. *Neurology* 2000; 54: 340-5.

Yerby M, El-Sayed Y. Pregnancy risks for the woman with epilepsy. In: Morrell MJ, Flynn K, eds. *Women with epilepsy*. Cambridge: Cambridge, United Kingdom, 2003: 203-14.

Walker M, Cross H, Smith S, *et al.* Nonconvulsive status epilepticus: Epilepsy Research Foundation Workshop Reports. *Epileptic Disord* 2005; 7: 253-96.