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Recurrent complex partial status epilepticus associated with tiagabine rechallenge

R. BROUNS and W. VAN PAESSCHEN
Department of Neurology, University Hospital Gasthuisberg, Catholic University Leuven, Belgium

We describe a patient who developed a complex partial status epilepticus (CPSE) after dose increase of tiagabine (TGB), that disappeared after dose reduction, but recurred subsequent to rechallenge with the original dose. This case report supports a possible causal link between TGB dosage increase and CPSE.

Case report

A 41-year-old man with a history of meningoencephalitis at the age of 17 months developed refractory temporal lobe epilepsy (TLE) at 9 years of age. He had on average four complex partial seizures (CPS) per month, and rare secondary generalized tonic-clonic seizures. He never had status epilepticus (SE). MRI showed left hippocampal sclerosis, ictal and interictal EEG revealed a left temporal lobe epileptic focus, and there was clear hypometabolism in the left temporal lobe on fluorodeoxyglucose-PET. Despite treatment with carbamazepine (CBZ) 1200 mg per day and lamotrigine (LTG) 400 mg per day, CPS persisted. LTG was gradually withdrawn over 3 weeks, while TGB was added and increased with 10 mg weekly. During the weeks prior to admission, the patient gradually experienced difficulties concentrating, increased somnolence and daily frequent blank spells, occasionaly with twitching of muscles. After the dose of TGB was increased to 60 mg daily, he experienced episodes of confusion, unresponsiveness and amnesia that could last for hours. At the time of admission, though, he was alert and oriented, CBZ level was 13 mg/dl (therapeutic range : 4-10), and an EEG showed generalized slow activity, which was felt to be consistent with intoxication. CBZ taper was started with 100 mg, and gabapentin (GBT) was added because of the worsening in seizures. On the ward, he often slept during the day, and his level of consciousness fluctuated between normal and lethargic. Several blank, unresponsive spells were observed. A repeat EEG on day three again showed generalised slow activity, but on day 6 runs of semirithmic anterior predominant delta and frequent left temporal lobe epileptic activity, which was – with hindsight – consistent with CPSE.

The patient was admitted to the video-telemetry unit, where the antiepileptic medication was reduced. TGB was decreased from 60 to 20 mg daily, CBZ from 1200 mg to 500 mg and GBT to 600 mg. Over the next few days, his mental state normalized. During one-week video-EEG monitoring, the patient experienced only one CPS and a diagnosis of CPSE could not be confirmed. At the end of the week, his medication was reinstated and he was discharged on TGB 60 mg, a reduced CBZ dose of 800 mg and GBT 900 mg daily. Three days later he was readmitted with an acute confusional state and mild twitching of his muscles. An EEG showed intermittent runs of rhythmic delta waves of high amplitude with anterior predominance and left temporal sharp waves, consistent with CPSE (Fig. 1). There was immediate electroclinical improvement after IV administration of lorazepam 4 mg. At this point, a paradoxical effect of TGB was suspected. Therefore, TGB was stopped immediately. The patient made a full recovery and with a follow-up of 4 months, CPSE did not recur.

Discussion

CPSE in patients with partial epilepsy and treated with TGB has been reported in (Balslev *et al*., 2000 ; Eckardt and Steinhoff, 1998 ; Ettinger *et al*., 1999 ; Piccinelli *et al*., 2000 ; Schapel and Chadwick, 1996 ; Trinka *et al*., 1999). In these cases, a causal relationship with TGB use was suggested since CPSE developed days to weeks after an increase in dose of TGB and disappeared without recurrence shortly after dose reduction or discontinuation of TGB, as in our patient. Shinnar *et al*. (2001), however, questioned the association of TGB use and CPSE since the incidence of SE and CPSE in patients treated with TGB was not increased compared with patients treated with placebo in clinical trials. In their review of 13 cases of possible non-consulsive SE reported in clinical trials with TGB, they only diagnosed three of these

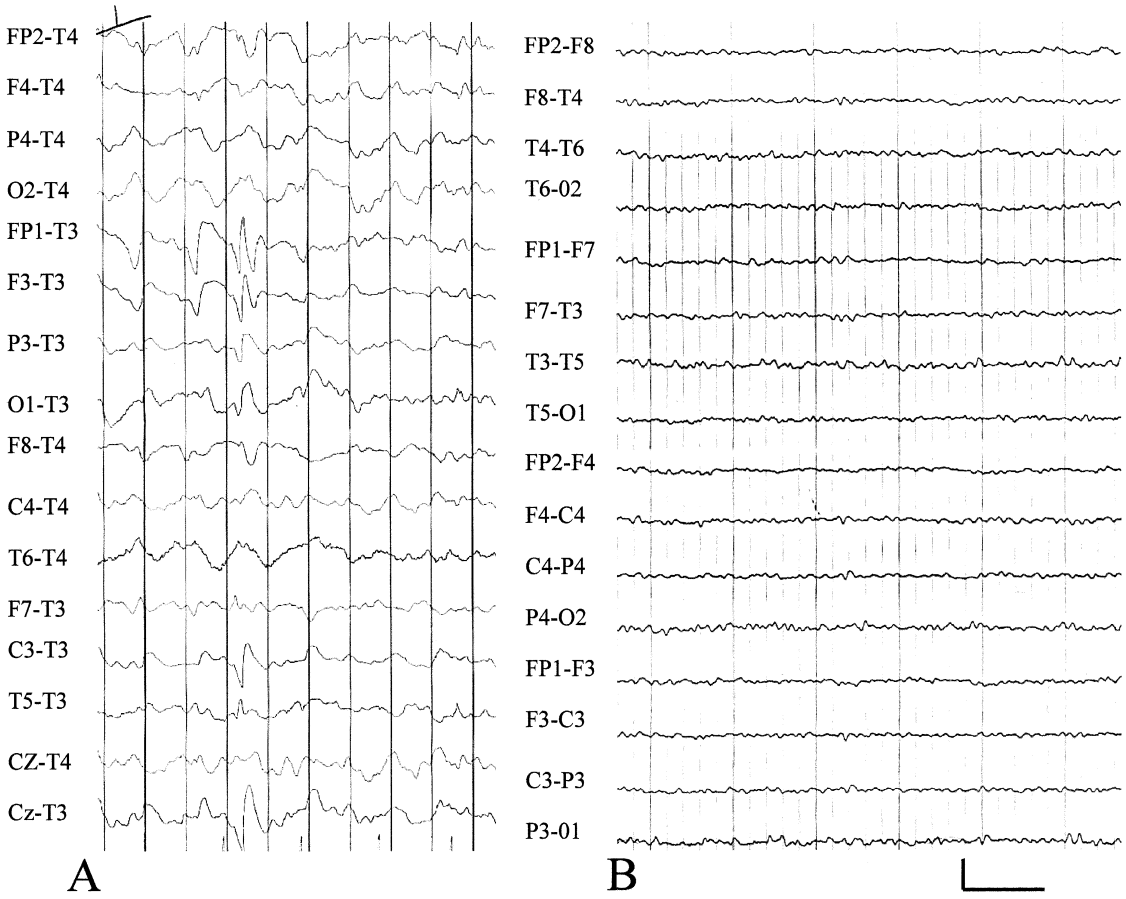

FIG. 1. — EEG recordings A) during the second episode of non-convulsive status epilepticus and B) 5 days later. A Referential montage. Run of left frontal high amplitude rhythmic delta and sharp wave followed by polymorphic slow. B. Bipolar longitudinal montage (double banana). There was a marked improvement in the EEG due to disappearance of the rhythmic slow and epileptic activity. This was associated with clinical recovery.

13 as having CPSE, based on history, electroclinical findings and response to IV lorazepam, as in our patient. The altered mental state in nine of these 13 patients was felt to be due to TGB intolerance. Eight of these 9 patients, however, did not receive IV lorazepam. We believe that part of the controversy whether TGB may cause CPSE is due to a lack of universally accepted criteria of CPSE. We conclude that a diagnosis of CPSE should be considered in a patient with an altered mental state on increasing, high doses of TGB, and that IV lorazepam administration under EEG monitoring should be part of the diagnostic work-up.

REFERENCES

BALSLEV T., ULDALL P., BUCHHOLT J. Provocation of non-convulsive status epilepticus by tiagabine in three adolescent patients. *Europ. J. Paediatr. Neurol.,* 2000, **4** (4) : 169-170.

ECKARDT K. M., STEINHOFF B. J. Nonconvulsive status epilepticus in two patients receiving tiagabine treatment. *Epilepsia,* 1998, **39** (6) : 671-674.

ETTINGER A. B., BERNAL O. G., ANDRIOLA M. R., BAGCHI S., FLORES P., JUST C. *et al.* Two cases of nonconvulsive status epilepticus in association with tiagabine therapy. *Epilepsia,* 1999, **40** (8) : 1159-1162.

PICCINELLI P., BORGATTI R., PERUCCA E., TOFANI A., DONATI G., BALOTTIN U. Frontal nonconvulsive status epilepticus associated with high-dose tiagabine therapy in a child with familial bilateral perisylvian polymicrogyria. *Epilepsia,* 2000, **41** (11) : 1485-1488.

SCHAPEL G., CHADWICK D. Tiagabine and non-convulsive status epilepticus. *Seizure,* 1996, **5** (2) : 153-156.

SHINNAR S., BERG A. T., TREIMAN D. M., HAUSER W. A., HESDORFFER D. C., SACKELLARES J. C. *et al.* Status epilepticus and tiagabine therapy : review of safety data and epidemiologic comparisons. *Epilepsia*, 2001, **42** (3) : 372-379.

SKODDA S., KRAMER I., SPITTLER J. F., GEHLEN W. Non-convulsive status epilepticus in two patients receiving tiagabine add-on treatment. *J. Neurol.*, 2001, **248** (2) : 109-112.

TRINKA E., MORODER T., NAGLER M., STAFFEN W., LOSCHER W., LADURNER G. Clinical and EEG findings in complex partial status epilepticus with tiagabine. *Seizure,* 1999, **8** (1) : 41-44.

W. VAN PAESSCHEN,
Department of Neurology,
UZ Gasthuisberg,
Herestraat 49,
B-3000 Leuven (Belgium).
E-mail : Wim.vanpaesschen@uz.kuleuven.ac.be