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# Unilateral continuous subclinical paroxysmal activity: an unusual finding in a patient with recurrent absence status

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**ABSTRACT –** We report a patient with a history of rare generalised tonic-clonic seizures and recurrent absence status who was diagnosed with a rare variant of idiopathic generalised epilepsy and absence status epilepsy. No other pathology was identified and MRI was normal. During a follow-up of 17 years, we recorded a single unilateral continuous, strictly subclinical, paroxysmal activity which lasted for at least several hours. No control was observed under treatment with phenobarbital, lamotrigine and topiramate. Absence status was aggravated with carbamazepine and generalised tonic-clonic seizures were not controlled with ethosuximide. Total seizure control was only possible with sodium valproate, which caused weight gain, and the patient has remained seizure-free for the past 10 years under 1,000 mg/d valproate and 200 mg/d topiramate. The recorded unilateral, long-lasting, subclinical spike-and-wave discharge is quite unusual for idiopathic generalised epilepsy and, in our opinion, occupies a transitional position between generalised and focal activity. *[Published with video sequences]*

**Key words:** absence status, idiopathic generalised epilepsy, unilateral EEG discharges, nonconvulsive status epilepticus

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EEG remains the most important tool to distinguish between focal and generalised non-convulsive status epilepticus. In absence status (AS), the EEG shows more or less continuous generalised, bilaterally synchronous, symmetric epileptic activity, usually maximal anteriorly. Granner and Lee (1994) analyzed EEGs in a large series of non-convulsive status epilepticus (NCSE) and found cases with an intermediate EEG state between focal and generalised NCSE.

We report a patient with a history of recurrent AS and rare generalised tonic-clonic seizures (GTCS) in whom we recorded a single highly unusual EEG with a unilateral continuous subclinical activity. To our knowledge, such long-lasting lateralized paroxysmal activity has not been reported before in a patient who otherwise fulfils the criteria of absence status epilepsy (ASE) (Genton *et al.*, 2008).

## Case study

A 29-year-old left-handed woman with normal neurological and mental status was diagnosed in September 1993

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with pharmacoresistant epilepsy. There was no family history of epilepsy. At age 14, a few days after a flue, she felt nauseous, stood up and suddenly fell. She may have had convulsions. She was confused and unresponsive for some hours thereafter. An EEG was recorded on the same day, while she was in the same state, and reportedly showed diffuse spike and waves (SW). Treatment was started with phenobarbital (PB), 100 mg/d, but was withdrawn gradually after three years with her neurologist's agreement. She then had a second seizure: she fell, presented twitching of the extremities and did not fully lose consciousness. A GTCS was diagnosed and PB was resumed until the age of 33. Under PB treatment she experienced recurrent episodes of clouding of consciousness, clumsiness, mental and motor slowing and variable memory problems. These episodes usually lasted at least several hours and occurred several times per year, mostly in the premenstrual period. PB was replaced by valproate (VPA) for several months in 1987, 1992 and 1993, resulting in full control but also in unacceptable weight gain. She returned twice to PB treatment with recurrence of episodes of confusion. CT scans were performed in 1978 and in 1988, both without any pathological findings, as well as MRI in 2008 which was also normal.

On her first referral, she was again treated with 750 mg/d VPA (blood level: 65 mg/L) and complained again of weight gain. The inter-ictal EEG showed sparse bifrontal rapid asymmetrical SW with left predominance. VPA treatment was stopped and EEG during afternoon sleep and on awakening was recorded two days later *(figure 1)*. The three-hour EEG showed repetitive, subcontinuous polyspike and SW discharges which were strictly unilateral over the left hemisphere and fragmented during brief light sleep periods, and at times during wakefulness, with reappearance of background alpha activity. The patient was fully oriented and both neurological examination and neuropsychological testing failed to show any abnormality. The recording was stopped while the abnormal activity was ongoing, and we were unable to guess the time of onset or offset, or the duration of this unusual EEG activity. As the patient was fully normal, no additional medication was given.

Because of the focal nature of the EEG changes, we prescribed carbamazepine (CBZ). The patient had at least two new episodes of confusion, one with 250 mg/d VPA (15 mg/L) and 600mg/d CBZ (6.1 mg/L) and two months later with 800mg/d CBZ (7 mg/L). The first AS lasted 5-6 hours and the second about 30 hours, which was much longer than usual. The patient was hospitalized. The EEG revealed continuous diffuse synchronous discharges of polyspikes and polyspike-waves (PSW) *(figure 2, see video sequence)*. AS did not react to 15 mg IV diazepam or 1,000 mg IV VPA, injected at 2 pm, when electrographic ictal activity persisted until recording was stopped at 6 pm, however, the patient reported feeling better later in the evening. Follow-up EEGs showed some slight slow activity over the left hemisphere on the following day, and a fully normal EEG the day after.

VPA was prescribed again. She was totally seizure-free for 2.5 yrs with 1,000 mg/d VPA (serum level of total VPA:

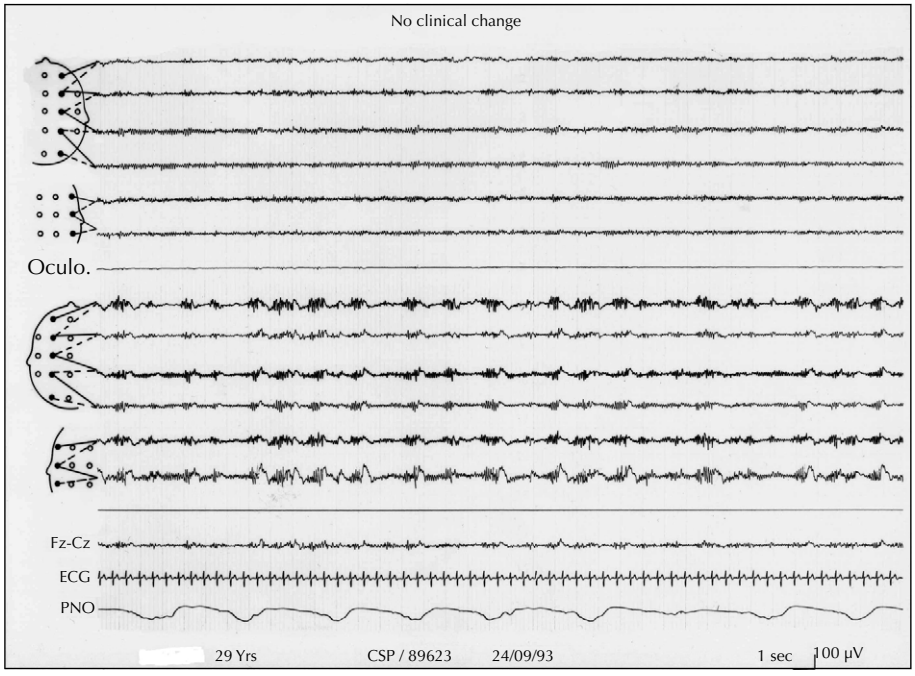


**Figure 1.** Subclinical continuous unilateral discharge recorded two days after interruption of VPA. The examination did not reveal any neurological or cognitive change. This state was recorded for three hours, without any indication of onset, offset and actual total duration.

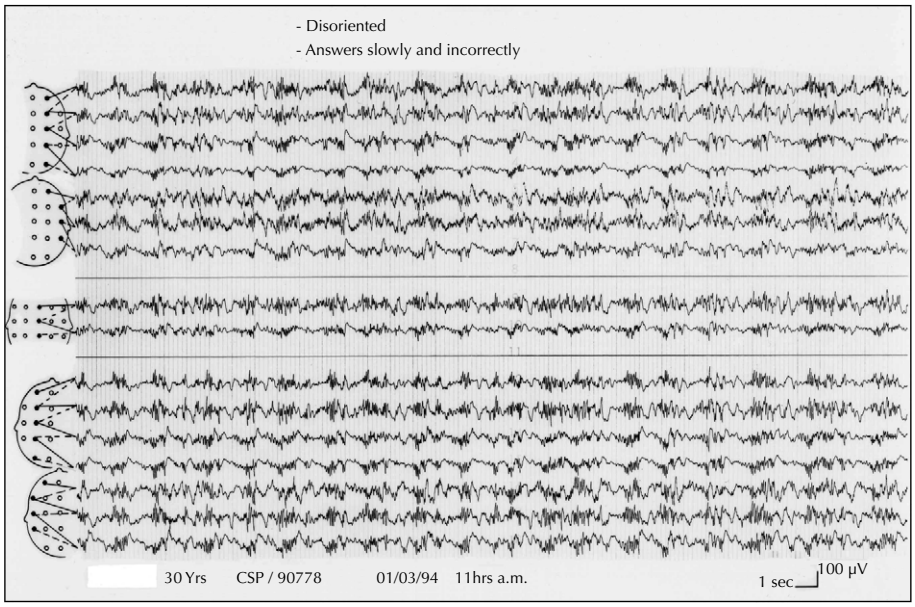


**Figure 2.** Absence status with diffuse EEG changes. The patient was partially responsive, disoriented and slow.

70-88 mg/L). She still complained of weight problems and on her insistence, VPA was gradually replaced with 750 mg/d ethosuximide (ESM) in July 1996. The patient experienced a GTCS. Treatment was again switched to VPA. In October 1997 lamotrigine (LTG) was added to VPA treatment and when a dose of 125 mg/d (7.1 mg/L) LTG was reached, VPA was tapered to the lowest effective dose. The patient experienced three new AS episodes over one year, when the doses of VPA were 250, 250 and 750 mg/d (37-54 mg/L) respectively. LTG was replaced with topiramate (TPM). Under TPM (50 mg/d) and VPA (750 mg/d) the patient had one AS in November 1999. VPA was increased to 1000 mg/d and TPM to 200 mg/d, resulting in weight loss of 12 kg and full seizure control. On June 2005 the blood levels of VPA were 72 mg/L (1,000 mg/d) and 6.2 mg/L for TPM (200 mg/d). In March 2010, no ictal events were reported and she continued to take treatment at the same doses. The clinical evolution under the various treatments is summarized in *figure 3*.

## Discussion

The diagnosis of AS in this case study was based on the following cardinal symptoms: spontaneous recurrence AS with onset at age 14 years, a frequency of several per year and aggravation by inadequate drugs. The clinical features are consistent with the criteria of AS associated with IGE (Agathonikou *et al.*, 1998); a state lasting for > 30 mins and characterized by clouding of consciousness varying from mild torpor to deep stupor.

Our patient also experienced GTCS, but did not experience any typical, short absence seizures or myoclonus. The classification of her epilepsy among the recognized (Commission on Classification and Terminology of the International League against Epilepsy, 1989) and recently described syndromes of IGE (Panayiotopoulos, 1997) is not easy. AS is considered a seizure type that may occur in various idiopathic absence syndromes in adults, with the highest prevalence in perioral myoclonia with absences and phantom absences with GTCS (Agathonikou *et al.*, 1998). Phantom absences may remain inconspicuous to both patient and physician for many years and crucial diagnostic examination is reported to depend on video-EEG monitoring during hyperventilation with breath counting (Koutroumanidis *et al.*, 2008). In spite of our attention directed to the cognitive functioning of the patient during repeated video-EEGs, we were unable to detect any phantom absences. Ictal EEG followed a typical pattern with diffuse continuous EEG changes. However, for the single occasion noted above, uni- or bilateral frontal ictal or inter-ictal changes, which could have been characteristic of NCSE of frontal origin, were never recorded. The mild inter-ictal focalization, which was observed only once in the wake of a typical AS, can be found in 35% of patients with IGE (Leutmezer *et al.*, 2002). There was no hint of focality in this patient.

All symptoms were well controlled by VPA alone at a daily dose not less than 1,000 mg/d. Ethosuximide controlled AS but did not prevent GTCS. AS persisted, without appearance of other seizure types, in the presence of phenobarbital, lamotrigine and topiramate, alone or in combination with VPA, at doses less than 1,000 mg/day, while CBZ aggravated AS. This pharmacological sensitivity is in concordance with IGE. Thus, we are inclined to

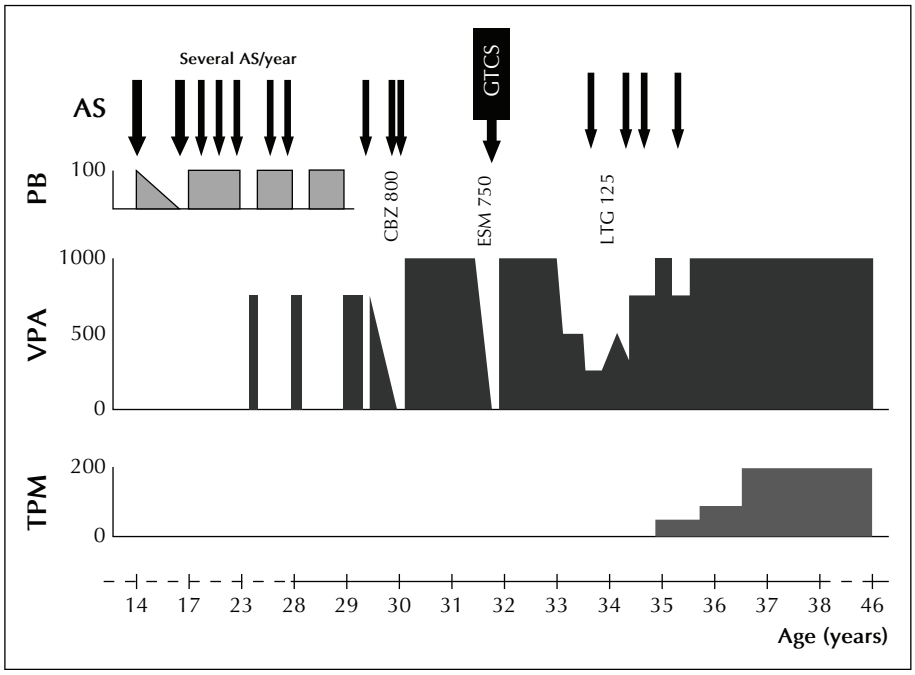


**Figure 3.** Pharmacological history, showing that full seizure control was obtained only with 1,000 mg/d VPA. Between ages 14 and 28, episodes of absence status occurred several times per year.

believe that our case presents a form of IGE, characterized only by frequent AS and rare GTCS, recently labelled "absence status epilepsy (ASE)" (Genton *et al.*, 2008).

Focal transformation of generalised seizures has been described in patients with IGE (Williamson *et al.*, 2009; Koutroumanidis *et al.*, 2009). Three possible mechanisms were proposed: focal cerebral dysfunction, focal/unilateral weakness of seizure terminating mechanisms and continuous firing of existing hyperexcitable cortical areas or systems after inhibition of the generalised cortico-thalamic oscillations.

In our patient we did not find any evidence of generalised activity preceding the reported unilateral paroxysmal discharges, which was much longer than that described in the cases of focal transformation of generalised seizures. Neither the patient nor her family reported obvious clinical changes associated with her usual AS. Since the structure of this unilateral continuous paroxysmal activity was very similar to that of the bilateral discharges with sub-continuous spike/polyspike wave, it may be interpreted as part of a generalised discharge rather than focal activity. A possible explanation for the probable mechanism to explain the generation of this activity is a "partial" or "unilateral excitation" of the oscillatory activity of the cortico-thalamic network, which determines absence seizures. During the AS, an impairment of the terminating seizure mechanisms, such as depolarizing current (Ih), is reported in thalamocortical cells (McCormick and Luthi, 1999). This could therefore determine both the AS and the continuous unilateral paroxysmal activity in our patient.

The lack of generalisation and the strict localization of this long-lasting discharge over the subdominant hemisphere may explain the absence of confusion as well as the preserved language abilities in the patient.

To our knowledge, the recorded unilateral, long-lasting, subclinical SW discharge is unique to ASE and occupies a transitional position between generalised and focal activity. For all practical purposes, in our opinion, this activity should be considered as a trait, however unusual, of IGE. □

## Legends for video sequence

### Part 1

Absence status with carbamazepine treatment. On the left are continuous diffuse discharges of polyspike-waves. Asked to count the fingers, she replies correctly ("four") after a delay. She obeys an order to raise her arms, but this simple gesture requires several trials and explanations. Note the absence of myoclonic jerks.

### Part 2

This is the same episode of absence status as in part 1. On the left, EEG abnormalities were recorded from the left hemisphere (the upper seven traces) and the vertex. Asked to count from 1 to 20, the patient complies after a delay. She is unable to count backwards from 20 to 1. Movements are slow but steady. Note the absence of myoclonus.

**Disclosure.**
None of the authors has any conflict of interest or financial support to disclose.

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