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Perioral myoclonia with absences and myoclonic status aggravated by oxcarbazepine

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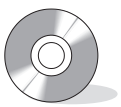
ABSTRACT – Perioral myoclonia with absences belongs to the "idiopathic generalised epilepsy syndromes in development", currently not yet cited in the ILAE classification. This epilepsy syndrome is associated with a seizure type that appears to be specific. Here, we report polygraphic recordings of this seizure type in a young boy, previously misdiagnosed with focal epilepsy. EEG and clinical features were useful to differentiate diagnosis of his seizures from other absence or myoclonic seizures. Interestingly, some seizures were associated with neck myoclonia. Home video recording of myoclonic status aggravated by inappropriate treatment is also presented. *[Published with video sequences]*

Key words: perioral myoclonia with absences, idiopathic generalised epilepsy, myoclonic status, neck myoclonia, oxcarbazepine, AEDs aggravation

Perioral Myoclonia with absences (PMA) is an epilepsy syndrome, described in 1994 by Panayiotopoulos, and is currently not yet recognized by the ILAE classification (Rubboli *et al*., 2009). This syndrome is characterised by a peculiar seizure type which consists of short absences with pronounced and constant rhythmic contraction of the perioral muscles, mainly involving the orbicularis oris. EEG or clinical asymmetry frequently leads to a misdiagnosis of focal epilepsy. Since the first series of six cases (Panayiotopoulos *et al*., 1994), one video case report was published in this journal (Bilgiç *et al*., 2001). In addition, two others with polygraphic data were more recently published (Baykan and Noachtar, 2005; d'Orsi *et al*., 2011). Here, we report a new case with polygraphic recordings of a patient's usual seizures and home video recording of myoclonic status aggravated by an inappropriate drug. Putative boundaries with other absences seizures with myoclonia are discussed.



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Case report

Family history was unremarkable. The patient was born at term after uneventful pregnancy and delivery. Psychomotor development was normal. He attends normal secondary school.

At the age of three years, he was admitted to the paediatric emergency department because of a first afebrile generalised convulsive seizure cluster. Within about two hours, he presented five seizures. EEG recorded the next day was normal. The child was treated with valproate for one year.

At the age of ten years, he experienced a clouded state with left hemifacial clonia, confusion and dysarthria. During the next year, his parents witnessed multiple short events, lasting for a few seconds. They described brief loss of contact with fixed gaze and constant twitching of the corners of the mouth, more pronounced on the left side. At times, the patient was aware of these episodes which preferentially occurred in the hour following awakening.

Subsequently, a first neurological workup was performed. Brain MRI was normal. EEG showed bilateral spike-waves with frontal predominance. The diagnosis of focal cryptogenic epilepsy was considered and oxcarbazepine (OXC) was introduced. Because of persistence of seizures, doses of OXC were raised to 1500 mg bid. The seizures became longer in duration, lasting about one hour, and one led to a generalised tonic-clonic seizure. Such status was video recorded by family members *(see video sequence 1)*.

At the age of 13, the patient was evaluated in our epilepsy centre. A polygraphic recording lasting for 24 hours was performed, including classic 19-channel EEG (10-20 montage) with video and surface EMG leads over the orbicularis oris muscle, sternocleidomastoid (SCM) muscle and in the medial posterior part of the neck. Background activity was normal during wakefulness and sleep. Interictal brief bursts of bilateral spike-waves and polyspike-waves were recorded, predominating sometimes over the left or the right hemisphere. Intermittent light stimulation was negative. Several usual seizures were recorded which were not induced by talking or reading. Impairment of consciousness was not systematically assessed. The patient was usually unaware of the seizures and activated the alarm button only after some seizures. The duration of seizures varied from two to ten seconds *(see video sequences 2 and 3)*. Rhythmic contractions of the perioral region were the predominant ictal symptom. On the video, the patient seems to pout, with protrusion of the lower lips and pursing of the lips, as well as depression and lateral movement of the commissure. Myoclonia systematically predominated on the left side. Muscles involved were the mentalis, depressor anguli oris, and orbicularis oris. The seizures were frequently associated with neck myoclonia, involving SCM muscle.

Ictal EEG consisted of 2.5 to 4-Hz generalised spike-waves and polyspike-waves *(figure 1)*. Polyspikes could contain more than three spikes. Epileptiform discharges were irregular, fluctuated in amplitude, and

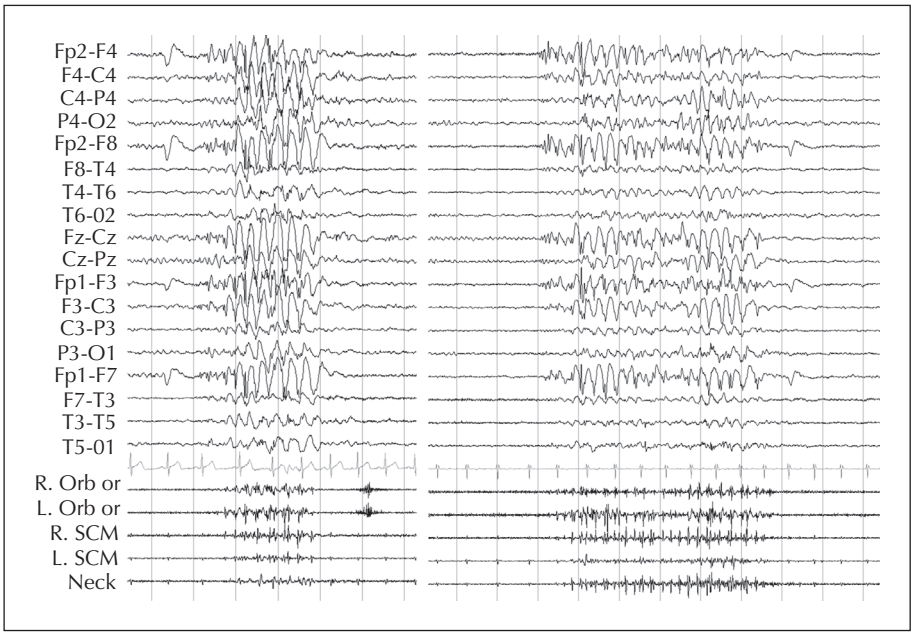

Figure 1. Polygraphic recording of two usual seizures that are presented in the video sequences.
Orb or: orbicularis oris, SCM: sternocleidomastoid muscle. The length of time between two vertical lines is one second.

were sometimes fragmented. The myoclonia recorded on EMG occurred at the same frequency as the spike-waves *(figure 2)*. Delay between the spike and onset of the myoclonus was between 15 and 20 milliseconds *(figure 3)*.

After this neurophysiological workup, a diagnosis of perioral myoclonia with absences was proposed and OXC was replaced by levetiracetam (LEV) at 2,000 mg bid. A few months later, seizure frequency decreased and he had no more generalised tonic-clonic seizures. However, occasional prolonged perioral myoclonia of about 45 minutes duration still persisted.

Discussion

Polygraphic data presented here has allowed us to clarify the ictal electroclinical semiology of PMA. In accordance with the first descriptions, duration of seizures varied between two to ten seconds and ictal EEG consisted of 2.5 to 5-Hz generalised irregular spike-waves and polyspike-waves, with frequent fragmentation. In comparison with typical absences, PMA were usually shorter, ictal epileptic discharges were less regular and polyspikes could contain more than three spikes. Each myoclonus was correlated with a time-locked spike component of a spike-wave complex. In our case, perioral myoclonia were often associated with neck myoclonia, occurring at the same frequency. Spreading of myoclonus to other facial muscles was clinically reported earlier in PMA, predominantly to the masseter. Recently, neck myoclonia with absences have been described in a series of three cases (Yang *et al*., 2009), of which one also exhibited perioral myoclonia. In these cases, ictal EEG was similar to PMA. Considering our data, it could be hypothesized that PMA and neck myoclonia with absences belong to a spectrum of the same seizure type.

Perioral EMG recordings showed that myoclonia were asymmetric. This was also reported in some of the clinical descriptions of PMA and in the previous

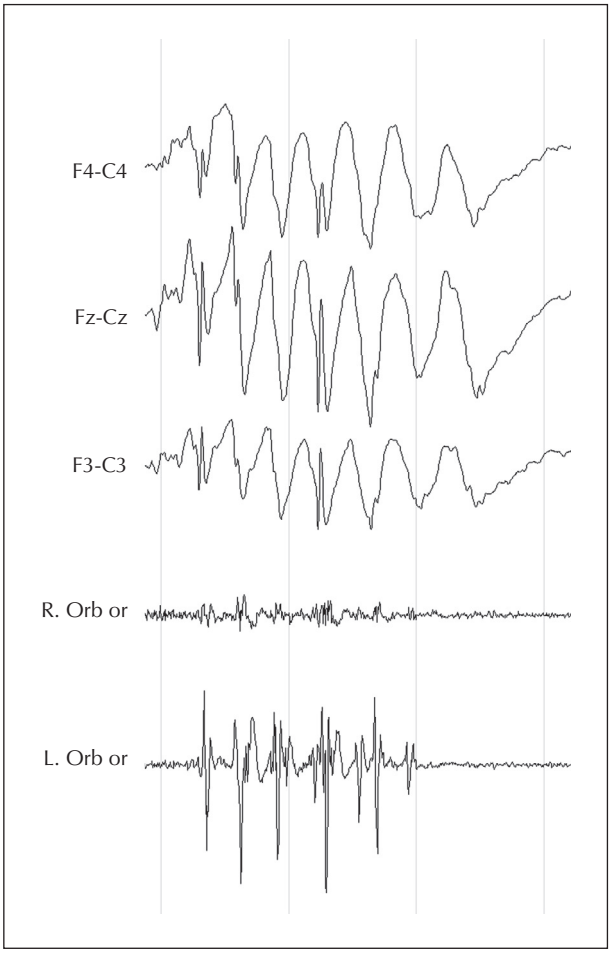

Figure 2. Recording of another usual seizure. Only fronto-central electrodes are shown to demonstrate the constant association between spikes and myoclonia.

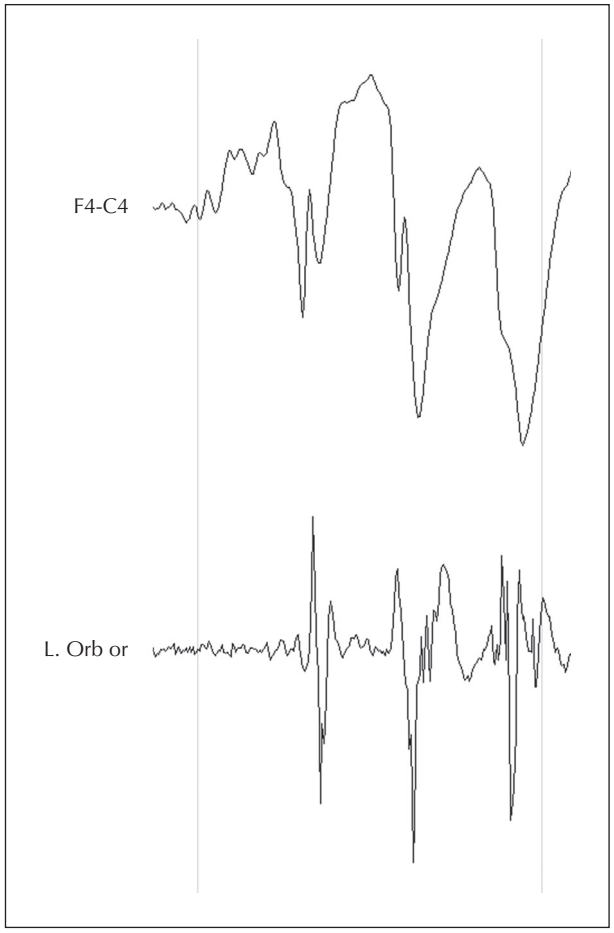

Figure 3. Time window is enlarged to show the delay between the spike and myoclonus.

polygraphic study. Asymmetry also occurs in a significant proportion of myoclonic seizures in the most common idiopathic generalised epilepsy (IGE) subtype, juvenile myoclonic epilepsy (JME) (Usui *et al*., 2005). Clinical and/or EEG lateralisation is the main reason for misdiagnosing PMA as focal seizures. This mistake is reported in the history of most PMA cases and is often a cause of clinical worsening because of inappropriate treatment.

As proposed by Panayiotopoulos *et al*. (1994), PMA seems to be a specific seizure type. Electroclinical features are specific and distinct from other absences associated with myoclonia:

i) in myoclonic absences, myoclonia may involve facial muscles but predominate in shoulders and arms (Bureau and Tassinari, 2005),

ii) in typical absences, perioral myoclonia are occasionally present but are not pre-eminent; in these patients, ictal EEG and prognosis are not different from typical absences without myoclonus (Capovilla *et al*., 2001),

iii) in eyelid myoclonia with absences, the perioral region is usually not involved (Caraballo *et al*., 2009).

Reflex perioral myoclonus may also be considered in differential diagnosis. It is the main seizure type in reading epilepsy and is also increasingly recognized in JME, induced by talking or reading (Mayer *et al*., 2006). Compared with PMA, the duration of reflex perioral myoclonus is shorter and they are not associated with impairment of consciousness.

PMA is not yet cited as a seizure type in the ILAE classification. In the most recent proposal (Berg *et al*., 2009), absences seizures are divided into three different groups: typical, atypical and absences with special features (including myoclonic absences and absences with eyelid myoclonia). In our opinion, PMA could be added to the third category.

The clinical history of our patient is compatible with criteria defining the syndrome of perioral myoclonia with absences, proposed by Panayiotopoulos *et al*. (1994): *i)* PMA is the main seizure type; tonic-clonic seizures are infrequent but constant; *ii)* epilepsy onset occurs during childhood or adolescence; *iii)* psychomotor development is normal; *iv)* seizures are difficult to treat; and *v)* episodes of status epilepticus are frequent.

Introduction or increasing dose of inappropriate AED is a frequent cause of myoclonic or absence status in IGE. In previous cases of PMA, seizure worsening by carbamazepine (d'Orsi *et al*., 2011) and precipitation of myoclonic status by phenytoin were noticed (Bilgiç *et al*., 2001; Baykan and Noachtar, 2005). The use of OXC in this syndrome has not previously been reported. OXC is known as a narrow spectrum AED that may aggravate absence and myoclonia in different subtypes of juvenile IGE and even precipitate absence status in juvenile absence epilepsy (Gelisse *et al*., 2004). In our case, switching OXC to levetiracetam, a large spectrum AED, led to the disappearance of tonic-clonic seizures, but without seizure freedom. Considering previous reports, drugs such as valproate, ethosuximide, lamotrigine and topiramate could also be effective to treat this syndrome.

In conclusion, this observation provides new data in favour of the existence of PMA as a distinct seizure type, defining a specific syndrome. Recognition of PMA is important, in particular, because of the risk of clinical worsening and possible recurrent status epilepticus following inappropriate treatment choice. □

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

Legends for video sequences

Video sequence 1

Extract from home video recording of myoclonic status. Myoclonic jerks are bilateral, predominate on the left perioral region, and spread to the shoulders and upper limbs. The patient is able to answer the questions of his mother, but with marked dysarthria. He deliberately shows the camera myoclonia in the arms. The patient subsequently says "what I have to say is blurred". At the end of the sequence his mother gives to him a tablet of lorazepam.

Video sequences 2 and 3

Usual seizures presented by the patient. Corresponding EEG recordings are shown in *figure 1*.

Key words for video research on www.epilepticdisorders.com
Etiology: idiopathic
Phenomenology: myoclonic seizure; absence (dialeptic) seizure; status epilepticus (non convulsive)
Localization: –
Syndrome: perioral myoclonia with absences

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