



Juvenile absence epilepsy: integrating photosensitivity and autonomic focal epileptic symptoms

Moisés León-Ruiz¹ · Milagros Merino-Andreu^{1,2} · Carlos Castañeda-Cabrero¹

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Dear Editor,

Panayiotopoulos syndrome belongs to self-limited childhood-onset focal epilepsies (SeLCOFE) and has recently been redefined as self-limited epilepsy with autonomic seizures (SeLEAS) [1]. Juvenile absence epilepsy (JAE) is included in idiopathic generalized epilepsies (IGE), representing 15–20% of epilepsies [2]. Photosensitivity is present in 17.9% of patients with IGE not treated with anti-seizure drugs (ASDs) [3] and focal symptoms (including autonomic) are found in 62.5% of patients with JAE [4]. Here, we present a remarkable JAE case with focal autonomic symptoms mimicking SeLEAS.

An 11-year-old girl presented to the emergency department of our hospital in March 2022 due to an abrupt clinical picture which occurred while dining at home (without watching television or using electronic devices), witnessed by her mother, lasting approximately 1 min, consisting of impaired awareness, loss of facial expression, ascending epigastric sensation, and vomiting. Her past medical history was otherwise unremarkable. Stroke code was activated and she was referred to another hospital, with normal neurological examination (pediatric NIHSS: 0) and vital signs on arrival.

She was hospitalized for 4 days. Blood tests (including SARS-CoV-2 RT-PCR RNA), chest X-ray, electrocardiogram, and cranial CT were normal, as were cytochemical and microbiological analysis of cerebrospinal fluid. An electroencephalogram (EEG) with video during wakefulness and sleep was performed (no images available, only the written

report), revealing a prevailing epileptiform activity over the posterior region of both hemispheres, predominantly left, as well as a type 4 photo-paroxysmal response (PPR), during intermittent photic stimulation (IPS), with no associated clinical changes. The patient was discharged with the diagnosis of a possible SeLEAS, without initiating anti-seizure medication (ASM).

Two months later, in the review at the Pediatric Neurology consultation of our hospital, no new spells like the previous one were reported. A new EEG with video was performed that day (Fig. 1A), where the findings of the previous EEG were replicated, although without a clear predominance of epileptiform discharges over posterior regions, PPR block with the blue color crystal, and without associated clinical manifestations. No ASM was prescribed as she had presented a single seizure and the possibility of a SeLEAS (which usually remits in 1–2 years after onset) [1] was not completely ruled out, but photoprotection (with polarized glasses with cobalt blue lenses) was recommended [5]. Two weeks later a 3T MRI of the brain with epilepsy protocol was performed, ruling out underlying structural pathology.

One month later, the EEG with video was repeated, under sleep deprivation, to increase the diagnostic yield, where in addition to the findings reported in the second EEG, an electro-clinical seizure was observed during hyperventilation, consisting of a typical absence (Fig. 1B). Therefore, in consensus with the patient's family, ASM (lamotrigine) was started, with progressive titration up to 25 mg/12 h orally, with adequate tolerance and response, achieving seizure freedom.

Photosensitive seizures are triggered by visual stimulation [6]. Photosensitivity is a genetically determined trait that can remain asymptomatic or manifest with seizures [7]. It is more common in the young (especially between 11 and 20 years) and female patients [8] and in specific forms IGE, such as juvenile myoclonic epilepsy (30–90%), childhood absence epilepsy (18%), JAE (8%), epilepsy with tonic–clonic bilateral seizures (TCBSs) (13%) and

✉ Moisés León-Ruiz
pistolpete271285@hotmail.com

¹ Pediatric Clinical Neurophysiology Unit, Department of Neurology, La Paz University Hospital, Paseo de la Castellana, 261, 28046 Madrid, Spain

² Pediatric Sleep Disorders Unit, Department of Neurology, La Paz University Hospital, Madrid, Spain

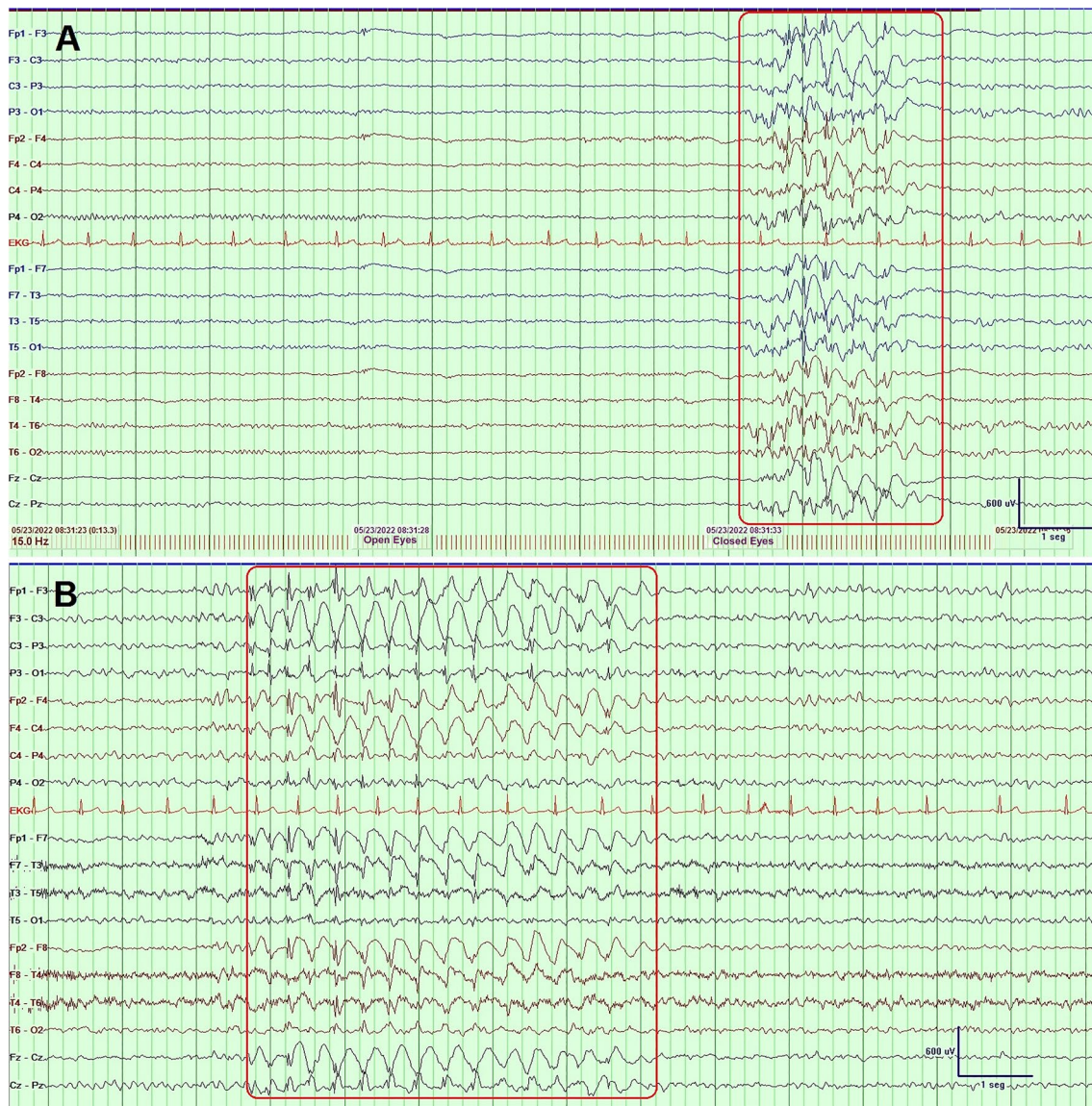


Fig. 1 **A** Second EEG during wakefulness and intermittent photic stimulation (in this case at 15 Hz): a type 4 photoparoxysmal response of the Waltz classification is identified after closing eyes, i.e., a paroxysmal generalized 3-Hz spike-and-wave and polyspike-and-wave discharge, of approximately 2 s duration and up to 400 μ V of amplitude (red rectangle). **B** Third EEG during wakefulness and hyperventilation induction (in this case with sleep deprivation): at 3 min a paroxysmal 3-Hz regular spike-and-wave discharge, with a duration of 5.2 s and abrupt onset and termination, and up to 500 μ V of amplitude is observed (red rectangle). In the simultaneous video

recording, the patient presented impaired awareness with absence of response to the question “Is everything all right?”, answering “yes” two seconds after the end of the discharge, with immediate return to normal activity, without other superimposed clinical features. Montage type in both EEGs: bipolar; Recording speed: 30 mm/s; Sensitivity: 30 μ V/mm; High frequency filter: 70 Hz; Low frequency filter: 0.5 Hz; Notch filter: with a cutoff frequency of 50 Hz. The space between two continuous vertical lines is equivalent to 1 s. *EEG*: electroencephalogram.

benign myoclonic epilepsy of infancy (BMEI) (10%). In these patients, the occipital cortex would show hyperexcitability, with an occipito-parieto-frontal spread, with the thalamus acting as a pacemaker (in the case of TCBSs), although the pathophysiology remains to be fully elucidated. Images with flashes > 20 lx (candelas/m²) at 3–60 (especially 15–20) Hz occupying 10–25% of the visual

field represent a risk factor, as are red flashes and oscillating streaks [6].

The associated symptoms are highly variable, ranging from mild subjective symptoms to palpebral myoclonus, TCBSs, absence seizures, etc. [6]. In the EEG, IPS can elicit a PPR, which consists of an electroencephalographic phenomenon as an expression of this photosensitivity [7].

In 1992, Waltz et al. [3] classified PPR into four types: type 1 (occipital spikes), type 2 (parieto-occipital spikes with biphasic slow wave), type 3 (type 2 with spread to frontal regions), and type 4 (generalized spike/polyspike-and-wave discharges), which represents the most pathological response [3, 5, 6]. Treatment includes a non-pharmacological approach (e.g., avoidance of triggering visual stimuli and the use of cobalt blue polarized glasses), as well as ASDs in cases refractory cases to the aforementioned approach [7].

When facing PPR identified in an epileptic patient with reported photosensitivity, the differential diagnosis should be established between photosensitive epilepsy, which is only composed of photoinduced seizures (BMEI, photosensitive occipital lobe epilepsy, etc.) and epilepsy with photosensitivity, which is characterized by photoinduced and spontaneous seizures: in case of neurodevelopmental involvement, epileptic encephalopathies (Dravet syndrome, progressive myoclonic epilepsies, etc.) should be ruled out, and if neurodevelopment is normal, IGE should be considered (as in our patient, whose first seizure was not photoinduced and whose second was) [5].

SeLEAS, first described in 1989 by Professor Chrysostomos P. Panayiotopoulos (“Tomis”), presents a series of

differential features compared to JAE (Table 1). It should be noted that for the diagnosis of SeLEAS, the presence of focal autonomic seizures is mandatory, with or without impaired awareness (nausea, retching and/or vomiting being present in 80% of cases; however, other autonomic symptoms may also appear, such as pallor, malaise, flushing, mydriasis, tachycardia–bradycardia, etc.), along with focal/multifocal epileptiform discharges predominantly in posterior regions, which increase during sleep and with ocular closure. Neuroimaging is usually normal, and should only be requested in case of red flags (e.g., age of onset > 8 years) [1, 9]. It does not usually require treatment given its tendency to remit spontaneously within 1–2 years of onset, but if remission does not occur, ASD of choice is carbamazepine, and the response is usually very successful (oxcarbazepine and levetiracetam have also been used as alternatives) [9].

Children with SeLEAS are not usually clinically nor electroencephalographically photosensitive. Although occasionally there may be some overt photosensitivity with small occipital spikes during IPS (which occurs when patients are in remission and occipital and/or multifocal discharges are controlled), it must rethink the diagnosis [10].

In our case, this fact, as well as the patient's age, made us question the initial diagnosis of SeLEAS issued in another

Table 1 Differential diagnosis between self-limited epilepsy with autonomic seizures (SeLEAS) and juvenile absence epilepsy (JAE).

Differential features	SeLEAS	JAE
Age of onset (usual)	1–14 years (3–6)	8–20 years (10–13)
Neurodevelopment	Normal	Normal
Frequency and duration of seizures	25% (1 seizure)/50% (≤ 6 seizures) Prolonged (10–50% > 30 min)	Less than daily 5–30 s (occasional longer seizures)
Impaired awareness	±	+ (partial)
Circadian distribution	Sleep (> 70%)	Sleep and wakefulness
Types of seizures	Focal autonomic (± OCD, hypotonic, clonic, BTCSSs, etc.)	Generalized (TASs* > BTCSSs > myoclonic) > febrile seizures > focal
Autonomic symptoms	+ + + (80% → Nausea, retching and vomiting)	+ (Epigastric visceral, chest tightness, cardiac, diaphoresis, flushing, heat, etc.)
Photoparoxysmal response	– (+ exceptional)	+ (25%)
Hyperventilation induction	–	+ (87%) / – (13%)
Interictal EEG	Sharp waves and high-amplitude (> 200 µV) multifocal spike-and-wave with onset in posterior regions	3–5.5 Hz generalized spike-and-wave
Ictal EEG	Onset in posterior regions (slow rhythmic activity + small spikes ± fast activity)	Regular 3–5.5 Hz generalized spike-and-wave (usually at 3 Hz)
Neuroimaging	Normal	Normal
Evolution	Remission in 1–2 years following onset	Good with antiseizure medication

Adapted from: Specchio N, et al. [1]; Hirsch E, et al. [2]; Seneviratne U, et al. [4]; Katyayan A, et al. [9]

The highlighted features in bold were those that led to rule out SeLEAS, and to consider the diagnosis of JAE

BTCSSs: bilateral tonic–clonic seizures; *EEG*: electroencephalogram; *OCD*: oculocephalic deviation; *TASs*: typical absence seizures

*TASs: absence seizures are mandatory. They have abrupt onset of impaired awareness, staring with loss of facial expression, interruption of activity, with/without oral automatisms, and immediate return to normal activity. Of note, loss of awareness is often less complete than in childhood absence epilepsy, where the patient may be able to respond to commands but has difficulty performing complex tasks. Subtle myoclonus may be seen [1]

hospital (probably due to overweighting of the vomiting), and consider JAE as a more probable diagnosis, taking into account that focal autonomic epileptic symptoms (e.g., visceral in the form of vomiting) are not uncommon in JAE [4] and was confirmed by the ictal EEG (with sleep deprivation).

In JAE, the age of onset is usually around 8–20 years (with a peak at 9–13 years). It is important to mention that >90% of patients have BTCs and 20% have absence status epilepticus [2], so it is important to use broad-spectrum ASDs, with valproic acid being the drug of choice, and lamotrigine and ethosuximide being used as the main alternatives, especially in women because of their potential adverse effects, alone or in combination [9]. Drugs whose main mechanism of action is the blockade of sodium channels (carbamazepine, oxcarbazepine, eslicarbazepine, phenytoin, etc.) are contraindicated because they can produce enhance neuronal membrane stabilization and hypersynchrony of neuronal discharges through a thalamo-cortical loop [11].

The conclusions to be drawn from this clinical case are the following: (1) Epilepsy is a frequent entity in pediatric age, with high clinical variability; (2) An electro-clinical syndrome is defined by characteristic features (epileptic semiology, age of onset, and electroencephalographic findings), which is going to allow guiding the treatment and predicting the prognosis in a more accurate way; (3) SeLEAS belongs to the SeLCOFE group and JAE to the IGE, according to the latest ILAE classification of 2022 [1, 2], with epileptic semiology, age of onset, EEG data (especially photosensitivity), and electro-clinical evolution being essential to differentiate between them; (4) Before making a diagnosis (e.g., an epileptic syndrome), especially in the pediatric age group (due to this clinical variability), attention should be paid to atypical data; (5) The electro-clinical evolution and the complementary tests (conventional EEG with activation maneuvers and simultaneous video recording) will allow achieving early accurate diagnosis and proper long-term ASM, avoiding ASDs that, being of choice for one entity, can induce and/or aggravate seizures of another.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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