

# Self-Limited Epilepsy with Autonomic Seizures (SeLEAS): A Retrospective Case Series

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## Abstract

**Objective** Self-Limited Epilepsy with Autonomic Seizures (SeLEAS), previously known by the eponymous Panayiotopoulos syndrome, is a benign focal epilepsy of the pediatric age group. It is characterized by nocturnal seizures with dominant autonomic features. Limited data from India exists on SeLEAS. We aimed to describe the clinical, demographic, and treatment-related features of SeLEAS.

**Methods** In this descriptive retrospective cohort study, we reviewed record of children who met criteria for SeLEAS. Each patient's clinical, demographic, electroencephalographic, neuroimaging, and treatment details were reviewed. Response to antiseizure medications was also recorded.

**Results** Twenty-three children with SeLEAS were enrolled (males = 18; 78.2%). Median age at onset was 4 (interquartile range: 2.5–10) years and median age at presentation was 6 (2.5–11) years. Focal seizures were observed in 65.2% ( $n = 15$ ) and 30% ( $n = 7$ ) had history of status epilepticus. Ictal/postictal emesis was observed in all patients. Occipital spikes on electroencephalography were seen in 78% ( $n = 17$ ). Four children had poor scholastic performance. Most (70%) of patients were well controlled on monotherapy, even with older antiseizure medications.

**Conclusion** This cohort shows the spectrum of clinical heterogeneity associated with SeLEAS. Although considered benign, occurrence of status epilepticus and poor scholastic performance among some of our patients suggests that some caution may be appropriate while prognosticating such patients. Seizures were well controlled with monotherapy.

## Keywords

- Panayiotopoulos syndrome
- benign occipital epilepsy
- autonomic seizures
- SeLEAS

## Introduction

Self-Limited Epilepsy with Autonomic Seizures (SeLEAS), formerly known as Panayiotopoulos syndrome, or early-

onset benign occipital epilepsy is an age-related focal epilepsy characterized by prolonged seizures with dominant autonomic features.<sup>1</sup> It was defined for the first time in 1989 by Panayiotopoulos, who described the triad of night-time

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seizures with eye deviation, vomiting, and electroencephalography (EEG) changes in the occipital region. SeLEAS has been reported to affect 6 to 13% of children who have had one or more afebrile seizures, and is the most common cause of afebrile nonconvulsive status epilepticus (NCSE) in childhood.<sup>2,3</sup> Seizures may not always be stereotypical and the hallmark autonomic manifestations maybe the only symptoms. Nausea and vomiting are the most prominent features followed by pallor, flushing, cyanosis, mydriasis/miosis, thermoregulatory and cardiorespiratory changes, incontinence, hypersalivation, intestinal dysmotility, etc. that may be misdiagnosed as encephalitis, syncope, migraine, sleep disorders, gastroenteritis, or nonepileptic seizures.<sup>2</sup> NCSE is a common occurrence in SeLEAS, in which the seizures are often extremely prolonged and classically take the form of autonomic status epilepticus.<sup>4</sup>

It is important for pediatricians and neurologists to know the heterogeneity of presentation of this epilepsy syndrome. In this retrospective study at a tertiary care center in India, we aimed to describe clinical characteristics, EEG features, and treatment among patients diagnosed with SeLEAS.

## Methods

We conducted a retrospective descriptive chart review-based study. A review of records was done of 850 children with epilepsy aged 1 to 18 years presenting to the Epilepsy Clinic of Kalawati Saran Children's Hospital, out of which 23 patients were identified as having SeLEAS. This study was done as a part of a larger study on epilepsy syndrome classification, conducted between May 2017 and October 2018, for which approval was obtained from the Institutional Ethics Committee. Informed consent was obtained from the parents.

The diagnostic criteria used for SeLEAS were in accordance with the International League Against Epilepsy definition.<sup>5</sup> We recorded details of clinical history and examination, pre- and perinatal antecedents, familial history of epileptic seizures, circadian distribution, seizure semiology and duration, EEG and neuroimaging, treatment, prognosis, and disease course, in addition to the demographic characteristics. A history of developmental delay or learning difficulties was based on reports of parents/caregivers as the children did not undergo standardized neurocognitive assessments. Magnetic resonance imaging was analyzed to assess for intracranial pathology. Treatment details, including number and type of antiseizure medications, were also recorded. Response to treatment was defined by seizure freedom or more than 50% reduction in seizure frequency on follow-up.

## Statistical Analysis

Data were entered into an Excel spreadsheet. Descriptive statistics were applied. Data were represented as frequency (percentage) or median (interquartile range [IQR]).

## Results

Our study included 23 children with SeLEAS (► **Table 1**). Our cohort showed a male preponderance (M: F = 3.6:1) ( $n = 18$ ;

**Table 1** Clinical characteristic of children with SeLEAS ( $n = 23$ )

Clinical features	<i>n</i> (%) / Median (IQR)
Males	18 (78.2)
Age at onset (median) (IQR)	4 (IQR: 2.5–10) years
Age at presentation (median) (IQR)	6 (IQR: 2.5–11) years
Focal seizures	15 (65)
Generalized seizures	8 (35)
Status epilepticus	7 (30)
Ictal/postictal vomiting	21 (100)
Positive family history	5 (22)
Past h/o febrile seizure	4 (17)
Occipital Spikes	17 (78)
Poor scholastic performance	4 (17)
Monotherapy	16 (70)

Abbreviations: SeLEAS, Self-Limited Epilepsy with Autonomic Seizures; IQR, interquartile range.

78.2%). The age at onset of epilepsy ranged between 2 and 11 years. The median age of onset was 4 (IQR: 2.5–10) years; the median age at presentation was 6 (IQR: 2.5–11) years.

All enrolled children had nocturnal seizures or seizures during early awakening. Most children ( $n = 15$ ; 65.2%) had focal seizures, of which 26% ( $n = 6$ ) children also developed bilateral tonic-clonic seizures. The remaining ( $n = 8$ ; 34.7%) had generalized seizures at presentation. Dyscognitive seizures were observed in 74% ( $n = 17$ ) of the children.

The seizure duration ranged from 10 to 20 minutes in our study. Two children (8.6%) had protracted seizures lasting for more than half an hour, while seven (30%) children fulfilled the definition for status epilepticus. Ictal/postictal vomiting was present in all children. Five children (22%) had a family history of epilepsy, while 17% children ( $n = 4$ ) had a preceding history of febrile seizures. Neuroimaging was unremarkable in all our enrolled cases. Occipital spikes were seen in 78% ( $n = 17$ ) children, while 17% ( $n = 4$ ) had a normal EEG and one child (4%) had multifocal discharges on EEG. Comorbidities in the form of poor scholastic performance after epilepsy onset were noted in 17% ( $n = 4$ ) children.

Seventy percent ( $n = 16$ ) of the children were managed with monotherapy. Epilepsy was well controlled on sodium valproate among 47.8% ( $n = 11$ ), phenytoin in 4 (18%), and 1 (4%) on levetiracetam. The remaining (30%;  $n = 7$ ) patients were managed with polytherapy. Among these, two children were treated with a combination of phenytoin and valproate. Levetiracetam, clobazam, carbamazepine, and topiramate were used in the remainder, as add-on therapy to phenytoin or valproate. Failure of valproate and phenytoin was noted in one child each, which was subsequently managed using monotherapy of carbamazepine and valproate respectively. Two children exhibited an atypical evolution to continuous spikes-wave during sleep (CSWS) and required steroid pulse therapy in addition to standard antiseizure medications. Both presented with poor academic problems and behavior

problems that started 6 to 8 months after the onset of seizures. The EEG showed electrical status epilepticus of sleep pattern. Both were treated with intravenous methylprednisolone 30 mg/kg/day for 5 days each month for 6 months. The clinical and EEG features showed improvement with this regimen.

## Discussion

SeLEAS is a childhood-related nocturnal epilepsy syndrome with occipital spikes. It differs from idiopathic childhood occipital epilepsy of Gastaut, which includes idiopathic photosensitive occipital lobe epilepsy with a later age of disease onset, and seizures in the awake state with visual symptoms. SeLEAS is the second most frequently described idiopathic focal epilepsy, second to Benign Epilepsy with Centro-Temporal Spikes (BECTS).<sup>6</sup> SeLEAS affects 13% of children aged between 3 and 6 years and 6% of children aged between 1 and 15 years, but its prevalence may be perhaps underestimated due to its misdiagnosis as encephalitis, migraine, gastrointestinal disorders, or as other non-epileptic paroxysmal disorder.<sup>2</sup> This study demonstrated a 2.5% prevalence of the subset of children presenting to a tertiary care center, and may not be truly reflective of normal population data due to referral center bias, and more complicated cases presenting to our clinic.

The usual age at onset is between 1 and 14 years with almost 76% of individuals reporting their first seizure between 3 and 5 years of age.<sup>7,8</sup> The median age of onset was also noted to be 4 years in our study. SeLEAS-associated seizures have been classically noted to take place either during early awakening or sleeping hours. Seizures with symptoms originating from the autonomic nervous system or the occurrence of status epilepticus are characteristic features of this early onset childhood epilepsy. Autonomic symptoms may be preceded by or coexist with headaches. Ictal/postictal vomiting is a consistent feature of this epilepsy and was found in all patients in our case series. A frequent symptom accompanying vomiting is one-sided lateral deviation of eyeballs with turning of the head to the same side, with disturbances in consciousness. Ictal vomiting has shown statistically significant association with benign childhood epilepsy with occipital spikes ( $p$ -value  $<0.001$ ) in comparison to BECTS.<sup>9</sup>

Focal onset seizures were seen in most of our patients, with some evolving to bilateral tonic-clonic seizures. Weir et al<sup>10</sup> ( $n = 7$ ) reported that all children in their series with SeLEAS presented with focal seizures, while various other studies reported a similar proportion (21–36%) of children with focal seizures with/without secondary generalization as seen in this study.<sup>2,11</sup> The incidence of status epilepticus is also reported to be variable, ranging from 4 to even 30%.<sup>12–15</sup> The slightly higher frequency observed in our series may possibly be due to referral center bias, as our center caters to complicated cases from the large catchment area of Delhi and the adjacent National Capital Region.

Seizures usually disappear 2 to 4 years after the first seizure, before the age of 16 without further risk of

recurrence in adulthood.<sup>8</sup> About 5 to 17% of patients with this epilepsy syndrome have a positive history of febrile seizures,<sup>14</sup> while we observed this in only one child. Preliminary studies implicated *SCN1A* mutations in few children but were not corroborated with further genetic analysis of children with SeLEAS.<sup>16,17</sup> Family history of epilepsy, observed in one fourth of our study population, was comparable to 30.3% observed by Caraballo et al<sup>11</sup> suggesting complex/polygenic influences.

Imaging studies are normal and helpful in differentiating from structural epilepsy. These are not mandatory but may be performed to rule out symptomatic occipital epilepsy. Most of our patients had occipital spikes on EEG. One patient had evidence of multifocal epilepsy on EEG. Presence of epileptic discharges in areas other than the occipital area maybe a prognostic sign for future evolution to other seizure type or epileptic syndrome. However, literature describes the presence of extraoccipital spikes (prefrontal, frontal, parietal, lateral temporal, or multifocal) in almost 25% of children with SeLEAS.<sup>14,18,19</sup> This multifocal hyperexcitable expanse has piloted the association of affected cortical areas to the hypothalamic autonomic centers and the limbic system, causing the expression of transient hyperactive central autonomic network, which is a key facet of SeLEAS.

The neurological examination and development along with neuroimaging of patients with SeLEAS are normal. It usually does not cause disorders of the psychomotor and intellectual development of the child, but poor scholastic performance was observed in 18% of our subjects. Fonseca et al<sup>20</sup> have, however, reported diffuse cognitive dysfunction in full-scale and performance intelligence quotient, visual attention, visual-motor integration, and verbal memory with a high incidence of internalizing behavioral problems. In addition, Germanò et al demonstrated deficits in writing, reading, arithmetic skills, and visual-spatial memory in children with SeLEAS.<sup>21</sup> They suggest neuropsychological and behavioral comorbidity in children with SeLEAS, necessitating the need for further studies with a larger sample size and long-term follow-up to authenticate this finding.

Medical professionals should be aware of the self-limiting nature of this epilepsy, which can be a cause of concern for the parents. Around 40% children have been reported to not require pharmacotherapy, influenced by several medical and social factors (low seizure frequency and severity, parental and child preference, nocturnal predominance) in a study in United Kingdom; a notion propagated by Panayiotopoulos et al themselves.<sup>13</sup> However, the question to treat children with idiopathic focal epilepsy syndromes remains unanswered as we are unaware whether regular antiepileptic therapy mitigates or exacerbates the cognitive and attentional comorbidities. Murine models have demonstrated that interictal focal EEG discharges lead to transitory regional cognitive dysfunction and impair long-term learning.<sup>22</sup> Recent studies suggest that interictal spikes in benign focal epilepsies impair memory consolidation in sleep.<sup>23</sup> Ten to twenty percent of SeLEAS patients face persistent autonomic status epilepticus that could be lasting for days that place them at great risk of developing life-threatening cardiorespiratory dysfunctions.<sup>24</sup>

The no-treatment practice also does not consider the costs associated with emergency room visits and admissions for unprevented seizures, therefore justifying the need for randomized controlled trials addressing the rationale for nontreatment.

Rare evolution of SeLEAS to other epileptic syndromes (Rolandic epilepsy, childhood absence epilepsy, juvenile myoclonic epilepsy, CSWS)<sup>11,25,26</sup> has also been reported. Generalized motor seizures including absences and myoclonic jerks or recurrent pharmacoresistant autonomic seizures may herald the changes in EEG findings of CSWS in children previously diagnosed as SeLEAS. Dooze and Baier have postulated that the childhood epilepsies with multifocal sharp waves are not independent but represent one clinical EEG spectrum of genetically determined childhood epilepsy (“hereditary impairment of brain maturation”).<sup>27</sup> Hirano et al<sup>28</sup> later hypothesized that acquired pre-existing neurobehavioral disorders or cerebral disturbances cause atypical evolution of SeLEAS due to reduced seizure threshold. Pulse steroid therapy (intravenous methylprednisolone 30 mg/kg/day) helped in achieving seizure control in our children, but neuropsychological and behavioral morbidity was not amenable to treatment with steroids.

Evidence to validate the use of specific antiseizure therapy for SeLEAS is limited, despite widespread variation in practice. For childhood focal seizures, first-line monotherapy with levetiracetam, lamotrigine, lacosamide, oxcarbazepine, phenytoin, pregabalin, gabapentin, and topiramate is recommended. Alternative monotherapy includes carbamazepine or valproate, and coadjuvant therapy may include clobazam, lacosamide or one of the drugs used as monotherapy. García and Rubio reported recurrence of seizures in some SeLEAS patients being treated with valproate and further demonstrated that levetiracetam introduced as add-on therapy to these patients, and then as monotherapy made the children seizure-free for 2 to 3 years.<sup>24</sup> The current cohort, however, had well-controlled seizures primarily on valproate thereby potentiating its role in idiopathic focal epilepsies also. Older antiseizure medications like carbamazepine and phenytoin also were seen to provide a fair control to seizures due to SeLEAS. In a developing nation like ours, where availability and affordability of the newer antiepileptic drugs is a major concern, our study demonstrates the utility of the older generation drugs in therapeutics of SeLEAS. Lacroix et al<sup>29</sup> advised caution in using benzodiazepines to treat autonomic seizures and reported five cases with severe respiratory depression following their administration.

Our study is among the largest series from India describing SeLEAS. We screened 850 children from our high-volume center and were able to collect several patients. Our study is limited by its retrospective design. A referral center bias is also likely considering that our center receives several complex epilepsy cases. We also could not report long-term prognosis of these children. We also do not have robust data on the intellectual capacity of these children, which is an important emerging concern.

## Conclusion

SeLEAS is a common focal pediatric epilepsy syndrome in developmentally normal children. We observed characteristic features of nocturnal seizures, autonomic symptoms, and occipital spikes in most children in our cohort. The seizures were prolonged and occasionally progressed to NCSE. Neuroimaging was typically nonlesional. Patients had good response to both old and new antiseizure medications. While the epilepsy is classically self-limiting, some caution may be exercised in considering it to be a benign syndrome, since cognitive issues have been reported. Future studies may focus on the cognitive aspects and long-term outcomes of children with SeLEAS.

### Funding

None.

### Conflict of Interest

None declared.

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