**Diagnostic algorithm for children presenting with epilepsia partialis continua**

**Snehal Surana[1*], Thomas Rossor[1*], Jane Hassell[1], Stewart Boyd[2], Felice D'Arco[3], Sarah Aylett MPhil[1], Sanjay Bhate[1], Lucinda Carr[1], Krishna Das[1], Catherine Devile[1], Christin Eltze[1], Cheryl Hemingway[1,4], Marios Kaliakatsos[1], Finbar O'Callaghan[1,5], Prab Prabhakar[1], Robert Robinson[1], Sophia Varadkhar[1], J Helen Cross[1,5], Yael Hacohen[1,4]**

1. Department of Paediatric Neurology, Great Ormond Street Hospital for Children, London, UK.
2. Department neurophysiology, Great Ormond Street Hospital for Children, London, UK.
3. Department neuroradiology, Great Ormond Street Hospital for Children, London, UK.
4. Department of Neuroinflammation, Queen Square MS Centre, UCL Institute of Neurology, London, UK.
5. Developmental neuroscience, institute of child health, UCL, London, UK

**Corresponding Author:** Dr Yael Hacohen, Department of Neuroinflammation, Queen Square MS Centre, UCL Institute of Neurology, London, UK
Email: y.hacohen@ucl.ac.uk
Telephone: 020 7405 9200

**Key words:**

Rasmussen Encephalitis, Mitochondrial diseases, POLG-related epilepsy, Epilepsia Partialis Continua, Autoimmune epilepsy

**Number of pages: 22**

**Word count for paper: 3236**

**References: 22**

**Figures: 3**

**Tables: 2**

**ORCID Numbers:**

**Dr Rossor 0000-0001-5472-1813**

**Dr Hacohen 0000-0001-8490-9657**

**Acknowledgements**:

*The authors are grateful to Dr Ming Lim for his thoughtful comments on the manuscript. They also thank all the numerous primary physicians and allied health professionals caring for these children during their complex course of disease.*

**Disclosures:**

*All research at Great Ormond Street Hospital NHS Foundation Trust and UCL Great Ormond Street Institute of Child Health is made possible by the National Institute for Health Research (NIHR) Great Ormond Street Hospital Biomedical Research Centre. The views expressed are those of the authors and not necessarily those of the UK National Health Service, the NIHR, or the Department of Health. JHC is an NIHR senior investigator. The authors have stated that they had no interests that could be perceived as posing a bias or conflict.*

**Ethical publication statement**

*We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.*

**Summary**

**Objective:** To characterise a cohort of children with epilepsia partialis continua **(**EPC) and develop a diagnostic algorithm incorporating key differential diagnoses.

**Methods:** Children presenting with EPC to a tertiary paediatric neurology centre between 2002 and 2019 were characterised.

**Results:** 54 children fulfilled EPC criteria. Median age at onset was 7 years (range 0.6- 15), with median follow-up 4.3 years (range 0.2-16). The diagnosis was Rasmussen encephalitis (RE) in 30/54(56%), a mitochondrial disorder in 12/54(22.2%), MRI lesion positive focal epilepsy in 6/54(11.1%). No diagnosis was made in 5/54(9%).

Children with mitochondrial disorders developed EPC earlier; each additional year at presentation reduced the odds of a mitochondrial diagnosis by 26% (p=0.02). Preceding developmental concerns (OR 22, p<0.001), no seizures prior to EPC (OR 22, p<0.001), bilateral slowing on EEG (OR 26, p<0.001) and raised CSF protein (OR 16) predicted a mitochondrial disorder.

Asymmetry or hemiatrophy was evident on MRI at presentation with EPC in 18/30(60%) children with RE, and in the remainder at median 6 months (range 3-15) after EPC onset.

The first recommended diagnostic test is brain MRI. Hemiatrophy may permit a diagnosis of RE with unilateral clinical and EEG findings. For those children in whom a diagnosis of RE cannot be made on first scan but the clinical and radiological presentation resembles RE, repeat imaging every 6 months is recommended to detect progressive unicortical hemiatrophy and brain biopsy should be considered. Evidence of intrathecal inflammation (such as oligoclonal bands and raised neopterin) can be supportive. In children with bihemispheric EPC, rapid POLG testing is recommended and if negative sequencing mtDNA and whole exome sequencing on blood-derived DNA should be performed.

**Significance:** Children presenting with EPC due to a mitochondrial disorder show clinical features distinguishing them from RE and structural epilepsies. A diagnostic algorithm for children with EPC will allow targeted investigation and timely diagnosis.

**Key words:**

Rasmussen Encephalitis, Mitochondrial diseases, POLG-related epilepsy, Epilepsia Partialis Continua, Autoimmune epilepsy

**Key points**

- Epilepsia partialis continua (EPC) in children is rare and has a wide differential diagnosis
- Children with mitochondrial disorders demonstrate clinical features at presentation which distinguish them from other causes of EPC
- This study proposes an algorithm to guide timely and efficient use of diagnostic tests

## Introduction

Epilepsia partialis continua (EPC) was first described over 120 years ago by the neurologist Koževnikov in a series of four patients with mild hemiparesis and sustained myoclonic jerks in the paretic limb. It was later defined as "spontaneous regular or irregular clonic muscular twitching affecting a limited part of the body, sometimes aggravated by action or sensory stimuli, occurring for a minimum of one hour, and recurring at intervals of no more than ten seconds"[1]. The definition has been extended to include non-motor phenomena in some studies[2]. The typical semiology of EPC involves repetitive myoclonic jerks that may be regular or irregular, predominantly involving distal rather than proximal muscle groups, and may be exacerbated by physical or mental exertion. Although attenuated by sleep, EPC normally persists[1].

The pathological processes that underlie EPC are heterogeneous and may differ between adults and children. Rasmussen's encephalitis (RE) is strongly associated with the development of EPC and is reported as the commonest cause of EPC in childhood[3]. EPC has also been widely reported in the context of POLG related disease[4, 5]. In a case series of 51 children with EPC more than half were diagnosed with inflammatory or immune mediated conditions including RE[3]. The next largest group comprised children with metabolic disorders, with the remainder comprising vascular aetiology, structural lesions, and those in whom no cause was found[3].

The wide differential diagnosis in children presenting with EPC, and the unavoidable delay in diagnosis of several of the more common aetiologies, creates challenges in the management of these children and appropriate counselling of families. The objective of this study was to identify clinical features at presentation with EPC predictive of common diagnostic

categories and develop a diagnostic algorithm for children with EPC that can guide targeted investigations, improve diagnosis and enable informed counselling of families.

**Methods**

All children diagnosed with EPC fulfilling the criteria above[3] prior to 18 years of age who were managed at Great Ormond Street Hospital between 2002 and 2019 were identified from the neurophysiology database. This database includes the neurophysiology reports of all patients who had EEG in our centre. Demographic information, clinical features at presentation, discharge and follow-up, and results of laboratory investigations, neuroimaging and EEG were compiled. CSF parameters were dichotomised to normal or elevated (white cell count >5/mm$^3$; protein >0.4g/dl; lactate>2mmol/l). EEGs had been performed in accordance with national guidelines[6] (www.bscn.org.uk; 30 minutes for awake EEG and 60 minutes for sleep with an EMG).

All available MRI scans were reviewed. The initial report provided by a paediatric neuroradiologist of the first MRI performed after diagnosis with EPC was used for data collection, without further review of scans to avoid bias introduced by additional retrospective scrutiny. Where scans had been performed prior to presentation with EPC comparison with earlier scans was included.

Statistical analysis was performed using the commercially available software SPSS Version 24 (IBM, CA) except calculation of odds ratio confidence intervals which were performed using Prism 8 for Mac (Graphpad LLC). Nonparametric statistical tests (Mann–Whitney or Kruskal-Wallis tests) were used for continuous distributions, and Fisher's exact test was used for nominal data when comparing groups.

Clinical and neurophysiological parameters were compared across groups (see Table 1) using Kruskal-Wallis for continuous or ordinal variables, and chi-square test for dichotomous variables. Clinical features and investigation results were converted to dichotomous outcomes where appropriate.

To explore potential predictors of diagnosis, those variables that differed with statistical significance of 0.1 across groups were identified.

Cases were coded as a diagnosis being present or absent, with each potential predictor as previously identified tested using Fisher's exact test against each diagnosis. Odds ratios and confidence intervals were calculated using the Baptista-Pike method. Statistical significance was taken at 0.05.

**Ethical approval**

As the data analysis was retrospective and no additional data were collected beyond that required for standard medical care of the patient, a full ethics review under the terms of the Governance Arrangements of Research Ethics Committees in the UK was deemed not necessary by the study team. Any data not published within the article will be shared by request from any qualified investigator

**Results**

*Patients*

A total of 54 children (32 females and 22 males) fulfilled the clinical criteria for EPC and were included in the study. Median age of first seizure was 5 years (range 1 month to 13 years), while median age at presentation with EPC was 7 years (range 7 months to 15 years). Patients were followed up for median 4 years (range 0.2-16 years). A final diagnosis of RE was made in 30/54 (55.6%). All children with a final diagnosis of RE fulfilled the criteria

proposed by Bien et al.[9] A final diagnosis of a mitochondrial disorder was made in 12/54 (22.2%). Eight of 12 had a pathogenic mutation detected on mtDNA or nuclear genes analysis; *POLG* (n=5), *m.3243A>G* (m=2) and *DMN1L* (n=1). One patient was diagnosed with Leigh's disease (complex-I deficiency on muscle biopsy) and three additional children had marked abnormalities on respiratory chain enzyme analysis.

A diagnosis of MRI lesion positive focal epilepsy was made in 6/54 (11.1%). Details of the lesions are provided below. No diagnosis had been made in 5/54 (9.3%) children all of whom were lesion negative on MRI. One child had EPC as part of Myelin Oligodendrocyte Glycoprotein antibody (MOG-Ab) associated disease. There was a history of developmental delay prior to the first seizure in 14/54 (25.9%) of the children and a history of seizures in 40/54 (74%). Clinical and paraclinical features stratified to the final diagnosis are summarised in **Table 1**.

The site of EPC is presented in **Table 2**. At presentation with EPC, EEG was abnormal in all but 1 child (53/54). For that child no diagnosis has as yet been made. The EEG abnormalities are summarised in **Table 2.** Bilateral discharges were seen in four children, three with mitochondrial disorders and one with RE. Bilateral slowing on EEG was seen in 9/12 (75%) children with mitochondrial disorders, in one child with RE, and one child with MOG antibody encephalitis. High amplitude delta with superimposed polyspikes (**Figure 1**) was seen in 3 patients with POLG mutation. EEG correlate with EPC was present in 28/54 (51.9%) children. In 27/54 an EEG correlate was apparent with conventional montages. Back averaging of EEG was performed in 8/27 children in whom no EEG correlate was apparent, which demonstrated an EEG correlate to EPC in one additional child.

CSF analysis was performed in 33 children. All patients had normal cell count. CSF protein and lactate were raised in 4/6 (67%) and 3/6 (50%) of patients with mitochondrial disorders respectively vs 2/18 (11.1%) and 0/17 patients with RE. Intrathecal oligoclonal bands and raised CSF neopterin were reported in 6/14 (42.9%) and 3/8 (37.5%) patients with RE (one patient had both OCB and raised neopterin) but were not seen in the 4 patients with mitochondrial disorders tested.

Mitochondrial DNA (mtDNA) analysis was performed in 18/30 patients who received a diagnosis of RE and all were negative for pathogenic variants. Eleven were not tested, and for one patient no information was available. Brain biopsy was performed in 24/30 children with a final diagnosis of RE. One biopsy was reported normal. The results of one biopsy are unavailable. The remainder had evidence of inflammation in keeping with a diagnosis of RE.

**Brain MRI at EPC presentation**

Evidence of hemiatrophy was seen on MRI at presentation with EPC in 18/30 (60%) patients all of whom received a final diagnosis of RE. Time from EPC to hemiatrophy in the other 12 patients was 6 months (range 3-15 months). Bilateral asymmetric atrophy was seen in one child. Unilateral signal abnormalities in the affected hemisphere were seen in 10/30 (33.3%) (**Figure 2**).

Bilateral signal changes were seen in 7/12 (58.3%) children with a mitochondrial disorder. One child with MELAS had evidence of both old and new infarctions in a non-vascular distribution; one had obstructive hydrocephalus with a persistent Blake's pouch cyst; one had a right parieto-occipital cortical abnormality alongside cerebellar atrophy which progressed over subsequent scans and one had a normal MRI brain at presentation.

The following abnormalities were identified in children with lesional focal epilepsy on initial scan: a Sturge-Weber malformation, left fronto-parietal cortical malformation suggestive of polymicrogyria, a temporal lobe cortical dysplasia, in one child with a history of hypoxic ischaemic encephalopathy extensive cystic change and cavitation within both cerebellar hemispheres in keeping with multicystic encephalomalacia and two children with subtle changes on MRI demonstrated on subsequent investigations with FDG PET to be focal cortical dysplasia.

Five children who remain without a formal diagnosis had normal MRI scans at presentation, one developed subsequent symmetrical volume loss. The child with MOG antibody encephalitis had extensive signal change in the cortex and subcortical white matter at presentation (**Figure 2**).

**Treatments and outcomes**

Across all groups the median number of different anti-epileptic drugs (AEDs) that had been employed was 5 (range 1-9). Immunotherapies were used in 25/27 children with RE in whom treatment data were available; corticosteroids (n=24), azathioprine (n=17), IVIG (n=15), two underwent plasma exchange and two received rituximab. Steroids were given to 4 of the 12 children with a final diagnosis of mitochondrial disorder, 3 of 6 children with lesional epilepsy, and 2 of 5 children in whom no diagnosis was made. The child with MOG antibody encephalitis received steroids, IVIG and plasma exchange.

Complete clinical outcome data were available in 53/54 children. One child with a mitochondrial disorder was lost to follow-up. The children with RE were followed up for median 5 years (range 1-13 years). Nineteen of the 30 with RE underwent hemispherotomy, with 14 (74%) going on to achieve seizure freedom, and the remaining 5 (26%) reporting a

reduction in seizure burden. Eleven children with RE continued on medical management and all 11 remain on AEDs. Ten have continued to have seizures, one has achieved seizure freedom.

Eight of the twelve children with mitochondrial disorder showed progressive deterioration and died. Time to death from presentation was median 1 year (range 3 months – 14 years). The surviving four children have ongoing seizures on AEDs, with EPC resolving in one. The median follow-up time of the surviving children is 1.2 years (range 4 months to 7 years).

The six children with MRI positive lesional focal epilepsy were followed up for median 8 years (range 3-16 year). Five underwent lesionectomy. None have achieved seizure freedom, but all have seen a greater than 75% reduction in seizure burden. One child with multicystic encephalomalacia has not undergone surgery and remains on AEDs.

Of the five children in whom no diagnosis was made, outcome data were available for four who have been followed-up for median 5 years (range 2-11 years). Two have achieved seizure control with medical management, two continue to have EPC despite medical management, both of whom have developed a movement disorder. The child with MOG antibody encephalitis continues to have seizures despite AEDs.

**Clinical predictors of diagnosis**

A number of factors were identified from univariate analysis that were predictive of a diagnosis of mitochondrial disorder. Preceding developmental concerns (OR 22 95% CI 4.1-88; $p<0.001$), and the absence of seizures prior to EPC (OR 22 95% CI 4.1-88; $p<0.001$) both predicted a mitochondrial disorder. Onset of EPC was earlier in children with a mitochondrial disorder than other disorders. With each additional year at presentation the odds ratio of a mitochondrial diagnosis reduces by 26% (95% CI: 5%-48%;$p=0.02$) Bilateral abnormalities on EEG were more commonly seen in children with mitochondrial disorders, with bilateral

background slowing being a stronger predictor (OR 26 95% CI 5.1-108; p<0.001) than bilateral ictal discharges (OR 14 95% CI 1.7-180; p=0.03).

Raised CSF protein (OR 16 95% CI 2.1-98; p=0.01) was predictive of a mitochondrial disorder.

The presence of seizures prior to onset of EPC was suggestive of a diagnosis of RE (OR 7.6 95% CI 2.0 – 28; p=0.004).

**Diagnostic algorithm**

We propose a diagnostic algorithm (**Figure 3**), applicable to any child presenting with EPC, which leads to four main diagnoses: RE, mitochondrial disease, MRI lesion positive focal epilepsy and lesion negative EPC.

The first recommended diagnostic test is brain MRI. Detailed Epilepsy protocol MRI will identify patients with lesion positive epilepsy which can be missed with other MRI protocols. On initial MRI unihemispheric cortical atrophy in combination with grey or white matter T2/FLAIR hyperintense signal and/or hyperintense signal atrophy of the ipsilateral caudate head may permit a diagnosis of RE with unilateral clinical and EEG findings. For those children in whom a diagnosis of RE cannot be made on first scan but the clinical and radiological presentation resembles RE, repeat imaging every 6 months is recommended to detect progressive unicortical hemiatrophy and brain biopsy should be considered. These may be expedited according to clinical course. Evidence of intrathecal inflammation (such as oligoclonal bands and raised neopterin) can be supportive. Exclusion of neurometabolic, inflammatory and mitochondrial causes is required.

Our data suggest that there are several strong predictors of a diagnosis of a mitochondrial disorder in children presenting with EPC. A prior history of developmental delay, an earlier onset of EPC and EPC as a first presentation of seizures are all predictive of an underlying mitochondrial disorder. Three children in our cohort had multifocal bilateral EPC, all of whom were diagnosed with POLG-related disease. In children with bihemispheric EPC, rapid POLG testing is recommended and if negative sequencing mtDNA and whole exome sequencing on blood-derived DNA should be performed. Raised protein and lactate would support a mitochondrial diagnosis.

Consideration of alternative diagnoses (e.g. inflammatory, neurometabolic and genetic) is recommended in the remaining minority of lesion negative EPC.

**Discussion**

In this study we present the clinical, EEG and radiological data for a cohort of children presenting with EPC. Based on these data we propose an algorithm to direct investigation and aid diagnosis, applicable to any child presenting with EPC.

EPC has been well described in children with POLG mutations alongside other movement disorders[7]. Characteristic EEG changes of rhythmic high amplitude delta with superimposed polyspike as previously reported in POLG related disorders[8] was seen in three children with POLG mutation only. While both background abnormalities and epileptiform discharges in the unaffected hemisphere have been reported in 25-62% of cases of RE 6 months after onset of seizures[9], this was only seen on the EEG at EPC onset in 2/30 of our children with RE suggesting this may be a later feature of RE.

EEG correlation with EPC was only observed in approximately half of our cohort. An absence of visually recognisable ictal surface EEG activity in EPC is well reported. In a large cohort of Chinese children with EPC, EEG correlation was suggestive of lesional focal epilepsy[10] and was observed less frequently in inflammatory aetiologies.

In this cohort, hemiatrophy was reported on the clinical scan at the onset of EPC in 20/30 patients with RE, including two of three children with no history of preceding focal seizures. In the context of the presumed diagnosis of RE this would suggest that the underlying progressive process starting prior to seizure or EPC onset. Progressive hemiatrophy has been previously reported in cases without seizure manifestations[11]. Approximately a third of children in this cohort demonstrated unilateral signal abnormalities on T2 and FLAIR imaging affecting both the cortical and subcortical regions. Although these may simply reflect the degree of seizure activity[12], evolution of these changes over time with gliotic changes seen on follow-up scans suggest these may be indicative of active brain inflammation[13]. Sequential imaging in those children with a non-diagnostic MRI at presentation demonstrated hemispheric atrophy within 15 months of presentation with EPC in all children. This supports repeated imaging when diagnosis remains unclear.
MRI at presentation was reported normal in one child with a mitochondrial disorder, and 4 of 5 children in whom no definitive diagnosis was made. Two children with lesional epilepsy due to focal cortical dysplasias had subtle abnormalities on initial MRI which were identified in retrospect. Both underwent subsequent FDG-PET scan to delineate the abnormality. Typical findings of RE on FDG-PET of hemispheric hypometabolism have been reported[14] suggesting there may be a role for PET scan to distinguish between a child presenting with early RE and lesional epilepsy although this has not been clinically evaluated.

Positive oligoclonal bands were seen in 6 out of 14 children with RE in whom they were tested, and in none of the four children with other diagnoses in whom testing was performed. Although positive oligoclonal bands may be seen in mitochondrial disorders and other non-inflammatory aetiologies[15] indicative of secondary inflammation, in the context of a child with EPC these are highly suggestive of RE and may be useful particularly in the context of equivocal imaging.

Despite regular screening for neuronal, glial and paraneoplastic antibodies only one child was diagnosed with MOG-Ab associated disease. MOG-Ab are now recognised as the most common cause of encephalitis in children[16]. Initially reported in children with ADEM and both monophasic and relapsing acquired demyelination[17], MOG-Ab has more recently also been recognised in the context of predominantly cortical encephalitis[18] presenting with seizures[19] as seen here. EPC has also been reported in children with anti-NMDA receptor encephalitis, although these children typically present with a severe encephalopathy with a complex movement disorder and NMDA receptor encephalitis is therefore unlikely to be the cause of EPC in isolation. Reports of some neuronal antibodies in patients with RE and mitochondrial disorders, even if they have the potential to be pathogenic are likely to be secondary phenomena resulting from epitope exposure, and not the primary cause of the disease.

AEDs have limited efficacy in the treatment of seizures in the context of RE[13] and this may be reflected in the large number of AEDs employed (median 5 AEDs). However, this poor response to AEDs was not limited to children with RE which suggests that irrespective of aetiology, seizures that manifest as EPC may be particularly resistant to pharmacological management.

Our study has limitations, of which the selection bias of a quaternary service providing epilepsy surgery is one. While we present a relatively large number of children with RE within our cohort, small numbers of children with other diagnoses limited the extent to which we could examine potential predictors. Including several potential predictors in a regression model was not statistically appropriate with the group numbers. Compared to other studies our cohort comprised a limited range of aetiologies which may reflect selection bias. Although previously reported in children with EPC[2, 3], we did not detect an infectious aetiology in our cohorts. Infective agent implicated in other studies have included Tick-borne encephalitis and Herpes Simplex encephalitis. Both subacute sclerosing panencephalitis and CNS tuberculosis can present with EPC and should be considered in endemic areas and in children who have not been vaccinated for measles. In a large multicentre European study comprising both children and adults with EPC alongside a number of structural lesions, other reported aetiologies included three with benign epilepsy with centro-temporal spikes, and two cases of Creutzfeld-Jakob disease[2].

While the differential diagnosis of EPC is wide, there are key features from the history and initial investigations which may predict the underlying disorder. Advanced brain imaging techniques, serial imaging and brain biopsy can be useful to further the diagnosis in MRI lesion negative EPC. New treatment algorithms may be proposed, both for controlling EPC which is usually drug resistant, and for modification of the underlying disease pathobiology. More rapid diagnosis with targeted investigations will reduce unnecessary investigations in children with mitochondrial disorders and inform appropriate counselling for the family.

| | Rasmussen | Mitochondrial | Lesion | Other | p-value |
|---|---|---|---|---|---|
| | **N=30** | **N=12** | **N=6** | **N=6** | |
| Male: Female | **14:16** | **4:8** | **1:5** | **3:3** | **0.50** |
| Age at first seizure (years) | **6 (2-13)** | **1.4 (0.6-10)** | **0.7 (0.1-6.5)** | **4 (0.3-13)** | **0.004** |
| Age at onset of EPC (years) | **7 (3-15)** | **2.7 (0.6-13)** | **6 (1-15)** | **6(2-13)** | **0.16** |
| Seizures prior to onset of EPC | **27/30** | **3/12** | **6/6** | **4/6** | **<0.001** |
| History of developmental delay | **1/30** | **9/12** | **2/6** | **2/6** | **<0.001** |
| Duration of follow-up (years) | **5 (1-13)** | **1 (0.2-14)** | **8 (3-16)** | **4 (2-11)** | **0.006** |
| Total number of AEDs used | **5 (3-9)** | **4 (1-7)** | **7 (6-8)** | **3 (1-7)** | **0.001** |
| **Outcome** | | | | | |
| Surgery | **19/27** | **0/12** | **5/6** | **0/6** | |
| Control on medication | **1/27** | **0/12** | **0/6** | **2/6** | |
| Partial control on medication | **2/27** | **2/12** | **1/6** | **2/6** | |
| Progression of condition despite treatment | **5/27** | **2/12** | **0/6** | **2/6** | |
| Died | **0/27** | **8/12** | **0/6** | **0/6** | |

Table 1: Clinical features and clinical course

| | Rasmussen | Mitochondrial | Lesion | Other |
|---|---|---|---|---|
| **Site** | N=30 | N=12 | N=6 | N=6 |
| Unilateral | 30 | 9 | 6 | 6 |
| Bilateral | 0 | 3 | 0 | 0 |
| Face | 17 | 7 | 2 | 2 |
| Arm | 12 | 8 | 4 | 5 |
| Leg | 17 | 2 | 2 | 0 |
| | | | | |
| **EEG at presentation with EPC** | | | | |
| Discharges | | | | |
| Unilateral | 21 | 5 | 4 | 3 |
| Bilateral | 1 | 3 | 0 | 0 |
| | | | | |
| Slowing | | | | |
| Unilateral | 22 | 1 | 3 | 1 |
| Bilateral | 1 | 8 | 0 | 2 |
| | | | | |
| EEG correlate with EPC | 16 | 5 | 4 | 3 |

Table 2. Site of EPC and EEG findings at initial presentation with EPC

Figure 1 Title: EEG demonstrating abnormalities in RE, POLG and Sturge-Weber syndrome

Figure 2 Title: MRI abnormalities in RE, POLG, Sturge-Weber syndrome and MOG-Ab associated disease

Legend: Axial T2 at presentation (A) and at 2-years (B) showing progressive left hemiatrophy and left frontal signal change (C) in a child with Rasmussen's encephalitis. Bilateral symmetrical signal abnormality within the deep cerebellar nuclei (D) and symmetrical restricted diffusion in the peri-rolandic cortical and subcortical areas (E) in a child with POLG

Left hemiatrophy (F) and prominent veins related to DVA and pial enhancement (G) in a child with Sturge weber syndrome. (H) Volumetric T1 demonstrating left frontal polymicrogyria.

Bilateral, assymetrical extensive signal change involving cortex and subcortical white matter (I) with restricted diffusion (J) in a child with MOG-Ab associated disease. Follow-up at 8month previous signal abnormalities have matured (K)

Figure 3 Title: A diagnostic algorithm for a child presenting with EPC

## Reference


1. Bien CG, Elger CE. Epilepsia partialis continua: semiology and differential diagnoses. Epileptic Disord 2008;10:3-7.
2. Mameniskiene R, Bast T, Bentes C, et al. Clinical course and variability of non-Rasmussen, nonstroke motor and sensory epilepsia partialis continua: a European survey and analysis of 65 cases. Epilepsia 2011;52:1168-1176.
3. Kravljanac R, Djuric M, Jovic N, Djordjevic M, Zamurovic D, Pekmezovic T. Etiology, clinical features and outcome of epilepsia partialis continua in cohort of 51 children. Epilepsy Res 2013;104:112-117.
4. Hikmat O, Eichele T, Tzoulis C, Bindoff LA. Understanding the Epilepsy in POLG Related Disease. Int J Mol Sci 2017;18.
5. Wolf NI, Rahman S, Schmitt B, et al. Status epilepticus in children with Alpers' disease caused by POLG1 mutations: EEG and MRI features. Epilepsia 2009;50:1596-1607.
6. Brodie MJ, Shorvon SD, Canger R, et al. Commission on European Affairs: appropriate standards of epilepsy care across Europe.ILEA. Epilepsia 1997;38:1245-1250.
7. Papandreou A, Rahman S, Fratter C, et al. Spectrum of movement disorders and neurotransmitter abnormalities in paediatric POLG disease. J Inherit Metab Dis 2018;41:1275-1283.
8. Rahman S, Copeland WC. POLG-related disorders and their neurological manifestations. Nat Rev Neurol 2019;15:40-52.
9. Longaretti F, Dunkley C, Varadkar S, Vargha-Khadem F, Boyd SG, Cross JH. Evolution of the EEG in children with Rasmussen's syndrome. Epilepsia 2012;53:1539-1545.
10. Li H, Xue J, Qian P, et al. Electro-clinical-etiological associations of epilepsia partialis continua in 57 Chinese children. Brain Dev 2017;39:506-514.
11. Bien CG, Elger CE, Leitner Y, et al. Slowly progressive hemiparesis in childhood as a consequence of Rasmussen encephalitis without or with delayed-onset seizures. Eur J Neurol 2007;14:387-390.
12. Yamazaki E, Takahashi Y, Akasaka N, Fujiwara T, Inoue Y. Temporal changes in brain MRI findings in Rasmussen syndrome. Epileptic Disord 2011;13:229-239.
13. Varadkar S, Bien CG, Kruse CA, et al. Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances. Lancet Neurol 2014;13:195-205.
14. Fiorella DJ, Provenzale JM, Coleman RE, Crain BJ, Al-Sugair AA. (18)F-fluorodeoxyglucose positron emission tomography and MR imaging findings in Rasmussen encephalitis. AJNR Am J Neuroradiol 2001;22:1291-1299.
15. Hacohen Y, Singh R, Forsyth V, Absoud M, Lim M. CSF albumin and immunoglobulin analyses in childhood neurologic disorders. Neurol Neuroimmunol Neuroinflamm 2014;1:e10.
16. Dubey D, Pittock SJ, Kelly CR, et al. Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. Ann Neurol 2018;83:166-177.
17. Hacohen Y, Banwell B. Treatment Approaches for MOG-Ab-Associated Demyelination in Children. Curr Treat Options Neurol 2019;21:2.
18. Armangue T, Olive-Cirera G, Martinez-Hernandez E, et al. Associations of paediatric demyelinating and encephalitic syndromes with myelin oligodendrocyte glycoprotein antibodies: a multicentre observational study. Lancet Neurol 2020;19:234-246.

19. Rossor T, Benetou C, Wright S, et al. Early predictors of epilepsy and subsequent relapse in children with acute disseminated encephalomyelitis. Mult Scler 2019:1352458518823486.