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Unexpected marked seizure improvement in paediatric epilepsy surgery candidates

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ABSTRACT

Purpose: Epilepsy surgery is performed based on the assumption that medical refractory epilepsy will continue. Rarely seizure freedom occurs before surgery is performed, while the patient is being evaluated as an epilepsy surgery candidate. The aim of this study was to describe the number of children withdrawn from an epilepsy surgery programme due to unexpected seizure improvement.
Methods: We retrospectively studied 173 children under 18 years with medical refractory epilepsy referred for epilepsy surgery between 1996 and 2010. Medical records were reviewed in 2012 and 2015.
Results: At the first evaluation point in 2012, 13 patients were withdrawn from the epilepsy surgery programme due to unexpected marked improvement. In 2015, 6 of them were still seizure free. They had unexpected seizure freedom due to change in AED treatment (n = 3) or after a febrile episode (n = 3). The mean number of years they had had seizures was 3.4 years (range 0.6–6.2 years) and the number of seizures at inclusion was 209 per month (range 6–750 per month). The duration of follow-up was 6.6 years after inclusion into the epilepsy surgery programme (range 4.0–13.0 years). The aetiology of the epilepsy for these patients was heterotopia (n = 1), focal cortical dysplasia (n = 3), infarction (n = 1) and unknown, with normal MRI (n = 1). They all had an IQ in the normal range. Two of the remaining 7 children were operated later.
Conclusion: Unexpected seizure control may occur during epilepsy surgery evaluation.

1. Introduction

Epilepsy surgery is performed based on the assumption that medically refractory epilepsy will continue. Surgery may be an option for a subset of the approximately 30% of paediatric patients with medically intractable epilepsy [1], defined as ongoing seizures despite a trial of two or more antiepileptic drugs (AEDs) suitable for the type of epilepsy, prescribed at maximum tolerated doses [2]. Expert consensus merits that early surgical intervention is critical, especially in infants with catastrophic epilepsy to prevent developmental arrest.

Up to 25% of parents have been found to be opposed to epilepsy surgery, but were more positive after factual information [3]. It is obvious that precise information on the chances of becoming seizure free with and without operation is important. The aim of this study was to retrospectively describe the clinical history of children withdrawn from the epilepsy surgery programme due to unexpected seizure improvement.

2. Methods

We retrospectively studied 173 children below 18 years with medical refractory epilepsy referred for epilepsy surgery between January 1996 and December 2010 at Dianalund Epilepsy Centre, Denmark (Table 1). Sixty-two of these later had epilepsy surgery. All children had been treated with 2–8 different relevant antiepileptic drugs at optimal doses at referral. All patients were enrolled in the evaluation programme consisting of evaluation at a tertiary epilepsy centre including one week of video EEG (electroencephalography), MRI (magnetic resonance imaging) scan, neuropsychological examination, and evaluation at a multidisciplinary conference. A subset of children also had interictal and/or ictal Single Photon Emission Computer Tomography (SPECT) or Positron Emission Tomography (PET). The same

Abbreviations: AED, anti-epileptic drug; CMZ, carbamazepine; GTK, generalized tonic-clonic seizure; EEG, electroencephalography; IQ, intelligence quotient; LEV, levetiracetam; LTG, lamotrigine; MRI, magnetic resonance imaging; PER, perampanel; PET, positron emission tomography; SPECT, single photon emission computer tomography; TPM, topiramate; VGB, vigabatrin; VPA, valproic acid.

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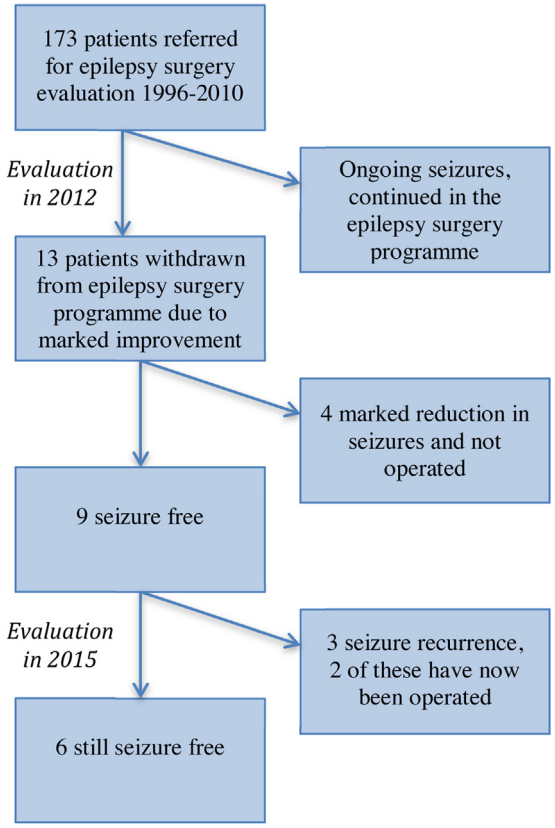
Table 1
Overview of the patients of the study.



paediatric neurologist (PU) followed all patients during the evaluation programme for epilepsy surgery. Due to limited resources including waiting lists the duration of the evaluation could last up to one year. Data was collected reviewing the medical records of the withdrawn patients. For the evaluation of unexpected seizure improvement the files were evaluated at two time points, first in March 2012 and later in April 2015. Data on febrile episodes, changes in AED treatment and seizure freedom were based on information from caretakers and medical records given at the outpatient clinic visit. A full protocol and results for patients operated in the same period has been published in Ref. [4]. The Danish Data Protection Agency approved the project with record number: 2015-41-4059.

3. Results

At the first evaluation point in 2012, 13 patients had been withdrawn from the epilepsy surgery programme due to marked improvement (see Table 1). Of these two boys and four girls were still seizure free in 2015, and described in Table 2. In three cases unexpected seizure freedom occurred within days after a febrile infection (cases 1, 3, 4 in Table 2). In the three remaining cases described in Table 2 seizure freedom was obtained after AED optimization. The time from change in AED to seizure freedom was not further specified in the journal files. The duration of follow-up ranged from 4.0–13.0 years after inclusion into the epilepsy surgery programme (mean 6.6 years). The age of epilepsy onset was 5.9 years (range 0–11.0 years) and age at inclusion in the epilepsy surgery programme was 9.0 years (range 5.7–13.5 years). The number of years with seizures was 3.4 years (range 0.6–6.2 years) and the number of seizures at inclusion was 209 per month (range 6–750 per month). The aetiology of the epilepsy for these patients was heterotopia (n = 1), cortical dysplasia (n = 3), infarction (n = 1) and unknown, with normal MRI (n = 1). They all had an IQ in the normal range.

Seven patients were seizure free in 2012 but not in 2015. Two of them have now been operated and one of them is seizure free. The other had marked fewer seizures for a period, but had recurrence of disabling seizures, and now after two epilepsy surgeries has marked fewer seizures again. The five remaining patients were not operated. Four still have rare seizures, and one now has a second period of seizure freedom due to a new AED combination. The aetiology of these seven patients was mesial temporal sclerosis (n = 2), polymicrogyria (n = 2), tuberous sclerosis (n = 1), cortical dysplasia (n = 1), infarction (n = 1).

4. Discussion

In this study we demonstrate that spontaneous and unexpected seizure control may occur also during evaluation for epilepsy surgery. Others have described spontaneous seizure freedom in patients regarded as having medically intractable epilepsy. West was one of the first to describe a patient with his syndrome

Table 2
Clinical characteristics of the patients that became seizure free.

Girl born 1990	Age at inclusion 11.4 y, had medically intractable seizures for 2.0 y (180 seizures/month, complex partial seizures), aetiology: dysplasia, 4 AEDs tried, was followed for 13.0 y since inclusion in surgery programme. Seizure free after measles infection. Currently treated with CMZ. IQ tested twice: 86/101
Girl born 1996	Age at inclusion 13.5 y, had medically intractable seizures for 2.7 y (6 seizures/month, GTK and focal seizures), aetiology: infarction, 2 AEDs tried, was followed for 5.0 y since inclusion in surgery programme. Seizure free with AED optimization (TPM). Currently treated with TPM & LEV. IQ > 70
Boy born 1997	Age at inclusion 10.9 y, had medically intractable seizures for 3.5 y (120 seizures/month, myoclonias, focal and GTK), aetiology: dysplasia, 5 AEDs tried, was followed for 6.8 y since inclusion in surgery programme. Seizure free after febrile episode with influenza-like symptoms. Treated with LTG & TPM since 2009. IQ 83
Girl born 2002	Age at inclusion 6.5 y, had medically intractable seizures for 6.2 y (750 seizures/month, focal seizures), aetiology: unknown/normal MRI, 3 AEDs tried, was followed for 6.2 y since inclusion in surgery programme. Seizure free after febrile episode with influenza-like symptoms. Treated with CMZ. IQ normal
Girl born 2003	Age at inclusion 5.9 y, had medically intractable seizures for 6.0 y (20 seizures/month, infantile spasms and focal seizures), aetiology: focal cortical dysplasia, 9 AEDs tried, was followed for 4.0 y since inclusion in surgery programme. Seizure free with AED optimization (VGB), all AED stopped 2013. IQ 73
Boy born 2004	Age at inclusion 5.7 y, medically intractable seizures for 0.6 y (180 seizures/month, GTK several times daily), aetiology: heterotopia, 5 AEDs tried, followed for 4.6 y since inclusion in surgery programme. Seizure free with AED optimization (VPA). Is currently tapering out of VPA as the last AED. IQ 100, mild learning difficulties

Abbreviations: AED: anti-epileptic drug; CMZ: carbamazepine; GTK: generalized tonic-clonic seizure; IQ: intelligence quotient; LEV: levetiracetam; LTG: lamotrigine; MRI: magnetic resonance imaging; TPM: topiramate; VGB: vigabatrin; VPA: valproic acid; y: years.