

Clinical profile of patients with rolandic epilepsy at a clinic in rural Maharashtra

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ABSTRACT

Purpose: To describe the seizure pattern, treatment strategies and outcome in a series of children with Rolandic seizures or childhood epilepsy with centrotemporal spikes. **Materials and Methods:** Patients were defined as Rolandic epilepsy if on electroencephalographic studies high voltage spike and waves were seen in centrotemporal areas, could be followed by slow waves, often activated on sleep and could shift from one side to other or be secondarily generalized. Typical (TRS) or benign were those with normal intellect. Atypical rolandic seizures (ARS) were those associated with neuroregression of language and cognitive milestones. Patients were treated with antiepileptic drugs if more than one episode occurred or the first episode was generalized status epilepticus. **Results:** Thirty-three patients were included over the period of eight years (2012-2020). There was male preponderance (21 males versus 12 females). Four patients (12.12%) later evolved into Landau Kleffner syndrome (ARS group). The mean age of onset of epilepsy in the TRS group (29 patients) was 7.2 (+/-2.2) with the youngest patient being 4 years and the eldest being 12 years. In the ARS group the mean age of onset was 5 yrs. (+/-1.41). In the TRS group, 23 (79.31%) patients were managed on monotherapy AED. Seventeen patients (58.62%) responded (remission) to carbamazepine monotherapy alone. Six patients (20.68%) could afford oxcarbazepine monotherapy and went in remission with this therapy. In the ARS group all patients required three drugs (valproate, clobazam and levetiracetam). By the end of the study period, 23/33 (75.75%) patients remained seizure free. **Conclusions:** Most patients with rolandic seizures have excellent prognosis being seizure free around puberty. The neurological outcome in most patients was normal.

Keywords: BECTS, benign childhood epilepsy, centro-temporal spike, Rolandic seizure

Introduction

Epilepsy is defined as two or more unprovoked seizures. Various types of epilepsy differ in aspects such as age at onset, semiology, electroencephalographic findings and outcome with or without treatment.^[1] Rolandic cortex is an area of the cerebral cortex that lies in and adjacent to the central sulcus (Rolandic fissure) which marks the boundary between the frontal and parietal lobes.

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Received: 05-07-2020

Revised: 13-09-2020

Accepted: 23-09-2020

Published: 08-04-2021

Rolandic epilepsy or childhood epilepsy with centrotemporal spikes (BCECTS) is characterized by typical semiology of hemifacial motor twitches involving the oropharyngeal muscles sometimes preceded by somatosensory symptoms and often develop into secondarily generalized tonic clonic seizures. The seizures are usually brief but status epilepticus is also known to occur.^[2] Their frequency is low, usually single lifetime episode to several episodes per day. Ictal manifestations occur more frequently (75%) during NREM (Non-Rapid Eye Movement) sleep, mainly at sleep onset or just before awakening. Typical range of onset ranges from 3 to 13 years with a peak at 7 to 8 years. Seizures stop by the age of 16 years usually.^[2] Although this epilepsy typically follows a benign remitting course; atypical

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How to cite this article: Sable S, Sable R, Tamhankar P, Tamhankar V. Clinical profile of patients with rolandic epilepsy at a clinic in rural Maharashtra. J Family Med Prim Care 2021;10:1263-6.

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_1355_20

types do exist.^{3,4} We report a case series of children with rolandic seizures observed over a period of ten years. Knowledge about rolandic seizures is important to primary care physicians so as to appropriately refer to neurologist for diagnosis, offer counseling to family about good prognosis and recognize red flags/comorbidities such as behavioral disorders or learning difficulties that can be appropriately managed.

Methods

The study was a retrospective analysis over the period from 2010 to 2020 in a clinic at rural setting. Patients were defined as having rolandic epilepsy by their typical semiology of hemifacial motor twitches and may be followed by secondarily generalized tonic clonic seizures. The electroencephalograph (EEG) was performed using the standard 10-20 electrode placement, in the interictal period and the pattern was recorded. EEG was performed at onset and whenever there were more than two seizures on treatment. Patient variables such as age at onset, number of seizures, types of anti-epileptic drugs (AEDs), response to AEDs, period to remission, persistence of seizures at the end of observation period of ten years. Patients with brain lesion on magnetic resonance imaging were excluded.

Patients with additional feature such as neuroregression were defined as the atypical group. Evaluation of academic difficulty or behavioral abnormality was also done. Academic underachievement was rated on a four-point score: Zero = absent, 1 = mild, reported by teachers but allowing normal schooling, 2 = moderate, requiring individualized help (1- year delay); 3 = severe, requiring special educational measures (more than 1-year delay). Behavioral problems (inattentiveness, hyperactivity, impulsivity, aggressiveness, hostile conducts) were scored as follows: Zero = absent, 1 = mild, reported by parents but causing minor harm to others, 2 = moderate, requiring psychotherapeutic or pharmacologic interventions; 3 = severe, provoking major difficulties despite adequate management. According to sum of academic and behavioral scores, evolution score was classified as benign (group I, score = 2 or less), complicated (group II = score 3 or more). The anti-epileptics were given as follows. The first drug of choice was carbamazepine which was started at a dose of 10 mg/kg/day in three divided doses and increased over a period of 2 weeks to maintenance dose of 20 mg/kg/day and maximum dose was 30 mg/kg/day. Sodium valproate was the first drug of choice when the seizure type was generalized tonic clonic seizure and the EEG pattern was generalized spike wave discharges or patient did not tolerate carbamazepine. The starting dose was 10 mg/kg/day (in 2 divided doses) and increased to maintenance dose of 20 mg/kg/day over a period of three days and maximum dose was 60 mg/kg/day. The first drug of choice was oxcarbazepine (starting dose of 15 mg/kg/day, maintenance dose of 25-30 mg/kg/day, maximum dose 40 mg/kg/day) in patients of higher socio-economic class since it was expensive prodrug of carbamazepine with fewer adverse effect and trice a daily dose. Other add on drugs were levetiracetam (starting dose 20 mg/kg/day in 2 divided doses increased to maintenance

dose of 30 mg/kg/day over a period of one week, maximum dose 60 mg/kg/day), clobazam (starting dose 0.2 mg/kg/day, maintenance dose of 0.4 to 0.5 mg/kg/day, maximum dose of 1 mg/kg/day). Monotherapy was given to those who remained seizure free and polytherapy was given when breakthrough seizures occurred on one/more drugs even at the maximum tolerated dose of the first drug. Seizure free remission in the TRS group was defined as absence of seizures for a period of two years and for the ARS group, remission was defined as a seizure free period of four years.

The persistence of seizures in patients after five years since onset of seizures was also calculated. Linear regression studies were performed to evaluate the factors determining the persistence of seizures after five years of age of onset of disease. String variables were converted into numerical variables. The factors considered were sex of patient (female = zero, male = 1), age of onset in years, presence of behavioral disturbances (presence = 1, absence = 0), academic underachievement score, behavioral difficulty score, composite score, number of seizures occurring in an individual in five years period and number of anti-epileptic drugs given to a patient.

Results

Clinical features

A total of thirty-three patients were included in the study. Twenty-nine patients (87.87%) were classified as having typical or benign rolandic epilepsy (TRS) whereas four patients (12.13%) had atypical rolandic epilepsy (ARS) with neuroregression as additional feature. The mean age of onset of the patients with TRS is 7.20 yrs. (+/-standard deviation of 2.2). The mean number of seizures in TRS patients observed during the study period is 3.14 (+/-1.77). The mean age of onset of the patients with ARS is 5 yrs (+/-1.41). In the ARS group, the mean number of seizures observed during the study period is 13.25 (+/-2.06). The type of seizure observed in the TRS group was nocturnal focal motor seizure with intact awareness in 15 patients (51.73%), nocturnal focal motor seizure with impaired awareness in 5 patients (17.24%) and generalized tonic clonic seizures in 9 patients (31.03%). The semiology included hemifacial seizures with eye deviation and/or headaches (27/33, 81.81%), hypersalivation (14/33, 42.42%), guttural sounds (10/33, 30.30%), dysarthria (5/33, 15.15%) and unilateral paresthesia (4/33, 12.12%). The type of seizure observed in the ARS group was generalized tonic clonic in all four patients. In 5 (15.15%) patients, there was post ictal Todd's paralysis. In the TRS group, three (two patients score 1 (mild), one patient score 2-moderate) (10.34%) patients had academic underachievement due to learning difficulties and behavioral abnormality (inattentiveness/hyperactivity) was present in four (13.79%) patients (three patients score 1, one patient score 2). None of the TRS group patients had both type of disturbances (academic as well as behavioral). In the ARS group, all patients had both type of disturbances academic as well as behavioral. The mean composite evolution score in the ARS

group was 4 (+/-0.82). All four patients in the ARS group had neuroregression after onset of seizures. These patients belonged to Landau Kleffner syndrome (LKS) group. Two of the patients in the TRS group (6.89%) and one of the patients in the ARS group (25%) had family history of seizures. All patients in TRS group were normal on clinical examination. The patients with ARS syndrome developed speech regression/aphasia

Tests and treatment aspects

The EEG pattern observed in the TRS patients was centrotemporal spikes in all twenty-nine patients and additional findings of parieto-occipital spikes was present in two patients (6.89%) and in another two patients (6.89%) generalized spike wave discharges were seen in follow up. The EEG pattern in the ARS group patients had centro-temporal spikes to begin with. However, in follow up these patients had continuous spike wave discharges during sleep (CSWS). These patients had normal developmental milestones before onset of seizures but had acquired aphasia after a mean period of 7.75 (+/-3.09) months after the first seizure.

Treatment aspects were noted with regards to anti-epileptic drugs (AED). In all thirty-three patients' anti-epileptic drugs were prescribed. In the TRS group, 23 (79.31%) patients were managed on monotherapy AED. Seventeen patients (58.62%) responded (remission) to carbamazepine monotherapy alone. Six patients (20.68%) could afford oxcarbazepine monotherapy and went in remission with this therapy. In two patient's sodium valproates was chosen as the drug of choice. In one of these patients, the EEG pattern showed generalized spike wave discharge and in the other patient carbamazepine was changed to valproate due to history of skin rash. In three (10.34%) patients' carbamazepine plus levetiracetam was used as dual therapy. In one patient in the TRS group three drugs valproate, clobazam and levetiracetam was used for therapy. In the ARS group since multiple seizures were occurring, three drugs (valproate, clobazam and levetiracetam) were used for therapy in all four patients. The mean duration of anti-epileptic drug in TRS group is 37.38 (+/-11.58) months whereas in the ARS group the mean duration is 90 (+/-15.49) months.

In the TRS group all patients except one (28/29, 96.55%) went into remission. Of the TRS group patients who went into remission, four patients had recurrence of seizures after stoppage of anti-epileptic drugs (persistent seizures after five years since age of onset of disease). Of these three patients one patient was on carbamazepine, second was on valproate and the third was on oxcarbazepine before stopping the drug. All three patients had either behavioral disturbances or learning difficulties. In the ARS group, after the diagnosis of Landau Kleffner syndrome a trial of oral prednisolone 2 mg/kg/day was given for two-three weeks with tapering over a period of further three-four weeks. A significant reduction in the number of seizures was observed. However, in the ARS group, none of the patients went into complete remission. For LKS, an intensive speech, occupational therapy, remedial education therapy was also employed to improve language skills.

The linear regression test to determine the most important factor for persistence of seizures at five years after onset showed the following results. The beta standardized coefficients were as follows: Presence of male sex (0.11, *P* value 0.307) age at onset (0.11, *P* value 0.327), presence of behavioral disorders (0.48, *P* value 0.008), academic underachievement score (1.12, *P* value 1.00), behavioral difficulty score (-0.41, *P* value 1.00), composite score (0.15, *P* value 1.00), number of seizures (-0.16, *P* value 0.548), number of anti-epileptics (0.00, *P* value 0.995). Thus, the most important determinant for persistence of seizures at five years after onset was presence of behavioral abnormality irrespective of the behavioral difficulty score.

Discussion

We reviewed the case series of Rolandic seizures published in recent times in medical literature. A recent study from United Kingdom^[5] showed incidence of rolandic epilepsy to be 5/100000 children (0 to 16 years) with 6% percent showing diagnosis of pervasive developmental disorder. Verroti *et al.* (2002)^[6] from Italy studied 64 cases of TRS and 11 cases of ARS. The mean age of onset of TRS was 8.2 years (group A) and ARS (group B) was 7.8 years. In group A, 24 patients were treated with carbamazepine and 6 with valproate. In group B, 8 patients were treated with carbamazepine and 3 with valproate. At the end of follow up 56/64 patients in group A had normal EEG whereas 6/11 patients in group B were normal. In group A, 7.8% had psychomotor disturbances (language delay) and in group B, 45.5% had developmental abnormalities.^[5] Tavares *et al.* (2005)^[7] from Portugal summarized their findings in children studied since 1989. They included 87 patients with mean age of presentation being 13.6 years much higher than that in our study. The patients had simple partial seizures in 69 cases and complex partial in 18 cases. Medication was administered to around 72% of their patients, rather than as 100 percent in our study. All patients had normal psychomotor development but some had learning difficulties. The higher usage of anti-epileptics in our study group was mainly because patient had multiple seizure before referring to our center and also because most parents were anxious about their children. No major side effects of the anti-epileptics were observed.

Dura Trave *et al.* (2008)^[8] studied 56 patients from Spain. Their mean age at diagnosis was 7.7 years. In all 62.5% were diagnosed during school age. Interictal EEG showed paroxysms in centrotemporal region, frequently unilateral (78.6%). Of all recurrences, 50.7% had it in the first year of diagnosis. Two cases progressed to epilepsy with continuous spikes and waves during slow-wave sleep/Landau Kleffner syndrome. Zhao *et al.* (2017)^[9] studied 316 cases from Shandong, China. Five percent cases were misdiagnosed as mesial temporal lobe epilepsy and other six percent cases had neuroradiological abnormalities leading to diagnosis of symptomatic epilepsy. Eight percent cases had cognitive deficits. In a retrospective study of 55 children with rolandic epilepsy, Metz-Lutz *et al.* (1999)^[10] showed significant decrease in scores of performances of two verbal subtests of

Wechsler Intelligence Scale for Children (WISC-R): Digit and vocabulary and two performance scale subtests: Block design and coding. Although, we could not systematically characterize the cognitive disturbance in our patients, we did show presence of scholastic disturbances in three patients of TRS group and all four patients of ARS group.

Regarding treatment, recent study from Iran^[11] proposed levetiracetam as monotherapy as an alternative to carbamazepine which can cause side effects such as skin rash and intolerance. However, we used carbamazepine alone in 58.62% of our cases without side effects and levetiracetam is more expensive. The usage of steroids in LKS was shown to be efficacious as in other studies. Santos *et al.* (2002)^[12] reported four cases with LKS. They had a mean age of presentation around 4 years. They showed good control of seizures with steroids regimen of 2 mg/kg/day. Other regimens used are the high dose regimen of 3 mg/kg/day as in Gallagher *et al.* (2006)^[13] and long duration of Sinclair *et al.* (2005)^[14] (1 mg/kg/day for 6 months, 1 year, then yearly).

Conclusion

Rolandic epilepsy is self-limiting disorder in most young children with remission by mid-adolescence. Most of the patients have good neurological and behavioral outcome with few patients having behavioral and scholastic impairments. Most of the patients are controlled with monotherapy. Few patients may evolve into atypical type like Landau Kleffner syndrome with significant neuroregression. Atypical rolandic epilepsy such as Landau Kleffner syndrome can show good response to steroids but complete remission may be evasive.

Key point

Patients with Rolandic epilepsy is a self-limiting disorder with good response to monotherapy and remission by mid-adolescence.

New message

In our study, the most important determinant for persistence of seizures at five years after onset was presence of behavioral abnormality.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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