A Case of Drug-resistant Epilepsy Associated with Ring Chromosome 20

Dear Editor,

Ring chromosome 20 syndrome (R20 syndrome) is a rare chromosomal disorder linked with epilepsy, described as early as 1972 and around 150 such cases have been reported in the existing literature.[1,2] R20 syndrome is characterized by childhood-onset intractable epilepsy, dysmorphic features, mental disability, behavioural issues and repeated non-convulsive status epilepticus (NCSE).[3,4] A cytogenetic test is required to confirm the diagnosis.

We evaluated a 21-year-old right-handed girl for drug-resistant epilepsy (DRE). Her events started at the age of 10 years. She had recurrent episodes of prolonged behavioural arrest lasting for 30–40 min during which she will be staring in unresponsive state throughout the event. The frequency of these events was 1–3 per day occurring during both awake and sleep. Her prenatal, birth, development and past medical history were unremarkable. She has no family history of epilepsy. Her scholastic performance was poor after the onset of epilepsy. On neuropsychological evaluation, her intelligence quotient (IQ) was 72, indicating borderline intelligence. No behavioural problems were reported. Her general and neurological examination was unremarkable. The magnetic resonance imaging (MRI) was normal and fluorodeoxyglucose-positron emission tomography (FGD-PET) was unremarkable.

She underwent long-term video electroencephalogram (EEG) to characterize the events. Many events were recorded. The seizure semiology was characterized by sudden onset of behavioral arrest with prolonged staring and immobile upper and lower extremities for 30–40 min associated with bilateral eye blinking. She was unresponsive to response testing throughout the event. Interictal EEG recording showed bi-frontal spike and sharp wave discharges [Figure 1a]. Ictal EEG recordings showed bi-frontal slow spike and wave discharges of 3–4 Hz frequency for 1–2 min followed by 5–6 Hz bifrontal spike and wave discharges which consistently evolved in frequency and amplitude for the next 30–40 min without any clear cut offset. The total duration of paroxysms was >40% of the recording length [Figure 1b].

A possibility of R20 syndrome was considered based on the above findings. To confirm the diagnosis, a chromosomal analysis of 30 lymphocytes was completed, which revealed a female karyotype with a translocation involving chromosome 1 and chromosome 12 along with a ring chromosome 20 in the mosaic condition in 14 of the 25 metaphases (56%) –46, XX, t (1;12)(q21;q11), mos r(20) [Figure 2]. Translocation involving chromosome 1 and 12 had not been linked to Epilepsy.

Previous treatment with valproic acid, oxcarbazepine and clobazam had no beneficial effect in reducing her seizure frequency. She was started on Valproic acid and Lamotrigine. At one year follow up, she had a significant reduction in seizure frequency with a frequency of 1–2 episodes per month.

R20 syndrome is characterized by distinct electro-clinical features such as (a) childhood-onset medically refractory

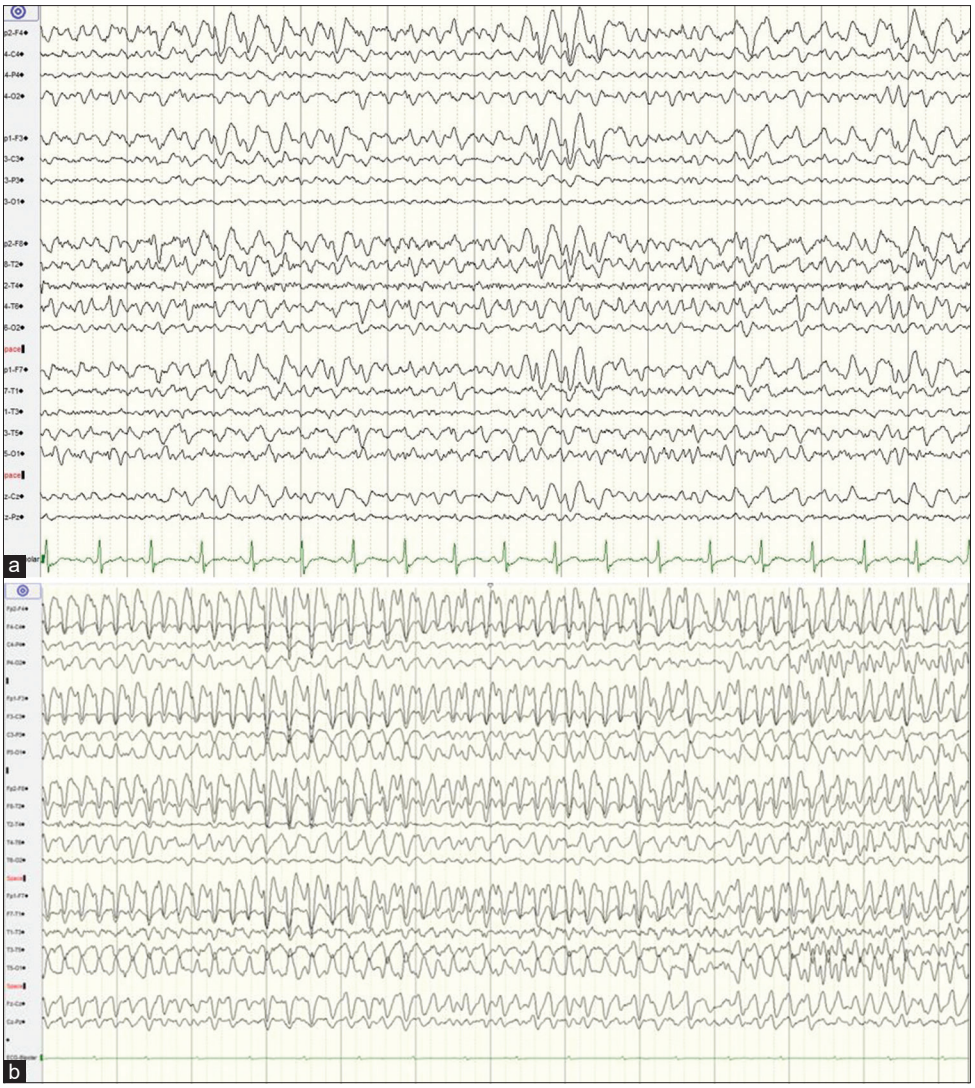

Figure 1: The inter ictal EEG (a) showing bifrontal spike and sharp wave discharges The ictal EEG (b) showing runs of high-voltage bifrontal slow spike and wave activity (low frequency: 1 Hz; high frequency: 70 Hz; sensitivity: 7 μV/mm; paper speed: 30 mm/s)

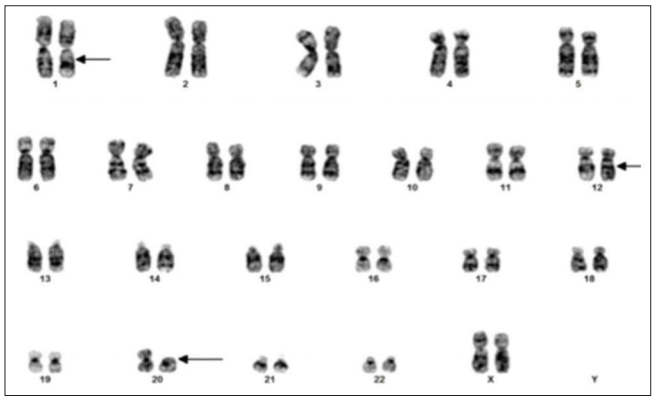

Figure 2: A female karyotype with a translocation involving chromosome 1 and 12 (arrows) and a ring chromosome 20 (arrow) is seen

epilepsy (b) mental disability (c) behavioral issues (d) dysmorphic features (e) focal seizures associated with oro-alimentary automatisms, frightened expression, altered consciousness with a staring gaze and frontal onset discharges of short periods (f) normal or near-normal background EEG activity with intermittent trains of constant theta waves in the fronto-central regions which may or may not be affected by eye-opening, level of consciousness or intravenous injection of diazepam (g) multiple episodes of NCSE with a classical EEG pattern characterized by serial runs of long-lasting unilateral or bilateral paroxysmal high-voltage slow waves with or without intermittent spikes over the frontal lobes which may spread over the scalp during the ictal event and (h) a normal brain MRI in most cases.[5,6]

Ring chromosomes have been identified for each of the 26 human chromosomes but only the ring chromosome syndromes that involve chromosomes 14, 17 and 20 are linked to epilepsy.[3] In R20 syndrome, epilepsy has an age-dependent course and has worse results when the initial age at seizure onset is earlier.[2] The EEG showing paroxysmal bursts during minutes with a total duration of paroxysms >20% of

the recording length can be considered as a landmark of ring chromosome 20 epilepsy syndrome.[6]

A higher percentage of cells with Mosaic chromosome 20 rings were seen to be related with earlier age of seizure onset, resistance to antiepileptic medication and more behavioural problems.[7] Our case has certain diverse features; despite a higher percentage (56%) of cells with mosaic chromosome 20 rings, she developed epilepsy at a later age (10 years) and she did not have any behavioural issues.

Radhakrishnan *et al*.[8] presented case series of 3 patients with different electroclinical syndrome diagnosed as R20 syndrome and Kalane *et al*.[9] reported a case of refractory epilepsy in a child with R20 syndrome. Valproic acid and Lamotrigine are considered to be the most effective combination of the treatment, although seizures remain to be refractory in most cases.[2] Ketogenic dietary therapy was reported as an effective and safe intervention for patients with R20 syndrome. There are reports describing benefit from vagal nerve stimulation in medically refractory cases of R20 syndrome.[10]

R20 syndrome is characterized by DRE, mental disability, multiple episodes of NCSE and prolonged bifrontal slow spike and wave activity on EEG. Chromosomal analysis is required to confirm the diagnosis. Atypical presentations of seizure semiology and NCSE can lead to delay in diagnosis. The syndrome should be suspected even in absence of behaviour disturbance and dysmorphic faces. Early identification can lead to better seizure control and prevent long-term cognitive deficits.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Anvesh Balabhadra, Mihir Parekh, Anuja Patil, Sita Jayalakshmi

Department of Neurology, Krishna Institute of Medical Sciences, Secunderabad, Telangana, India

Address for correspondence: Dr. Sita Jayalakshmi, Department of Neurology, Krishna Institute of Medical Sciences, 1-8-31/1, Ministers Road, Secunderabad, Telangana, India.
E-mail: sita_js@hotmail.com

References

1. Atkins L, Miller WL, Salam M. A ring-20 chromosome. J Med Genet 1972;9:377-80.
2. Vignoli A, Bisulli F, Darra F, Mastrangelo M, Barba C, Giordano L, *et al.* Epilepsy in ring chromosome 20 syndrome. Epilepsy Res 2016;128:83-93.
3. Elens I, Vanrykel K, De Waele L, Jansen K, Segeren M, Van Paesschen W, *et al.* Ring chromosome 20 syndrome: Electroclinical description of six patients and review of the literature. Epilepsy Behav 2012;23:409-14.
4. Inoue Y, Fujiwara T, Matsuda K, Kubota H, Tanaka M, Yagi K, *et al.* Ring chromosome 20 and nonconvulsive status epilepticus. A new epileptic syndrome. Brain 1997;120:939-53.
5. Ville D, Kaminska A, Bahi-Buisson N, Biraben A, Plouin P, Telvi L, *et al.* Early pattern of epilepsy in the ring chromosome 20 syndrome. Epilepsia 2006;47:543-9.
6. Freire De Moura M, Flores-Guevara R, Gueguen B, Biraben A, Renault F. Long-term EEG in patients with the ring chromosome 20 epilepsy syndrome. Epilepsia 2016;57:e94-6.
7. Giardino D, Vignoli A, Ballarati L, Recalcati MP, Russo S, Camporeale N, *et al.* Genetic investigations on 8 patients affected by ring 20 chromosome syndrome. BMC Med Genet 2010;11:146.
8. Radhakrishnan A, Menon RN, Hariharan S, Radhakrishnan K. The evolving electroclinical syndrome of "epilepsy with ring chromosome 20". Seizure 2012;21:92-7.
9. Kalane U, Datar C, Kalane S. Ring chromosome 20 syndrome-A rare chromosomal cause of refractory epilepsy in children. Int J Epilepsy 2017;4:87-9.
10. Chawla J, Sucholeiki R, Jones C, Silver K. Intractable epilepsy with ring chromosome 20 syndrome treated with vagal nerve stimulation: Case report and review of the literature. J Child Neurol 2002;17:778-80.

Submitted: 31-Dec-2020 **Revised:** 13-Jan-2021 **Accepted:** 18-Jan-2021
Published: 16-Apr-2021

DOI: 10.4103/aian.AIAN_1292_20