Case Report

Rare Epileptic Syndrome of Ring Chromosome 20 with Epileptic Encephalopathy: A Case Report

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The authors report the clinical features, electroencephalography (EEG), neuroimaging (brain magnetic resonance image-MRI), and cytogenetic findings of a young female patient with rare cytogenetic anomalies characterized by de novo 46, XX, r (20)(p13q13.3). The patient had a history of mild mental retardation, emotional liability and intractable epilepsy with non-convulsive status epilepticus. The MRI brain showed focal cerebral dysplasia over the left temporal region. The multiple seizures were refractory to antiepileptic medications and prolonged, confused state with or without a motor component. The continuous video-EEG monitor showed epileptiform discharges over bilateral frontal regions with frontal origin. The symptoms were relieved after midazolam infusion.

A patient who was present with intractable epilepsy with continuous frontal epileptiform discharges, mental retardation, abnormal behavior, without dysmorphic features should be suspected of chromosomal abnormalities especially ring chromosome 20.

Keywords: *Ring chromosome 20, Epileptic encephalopathy, Non-convulsive status epilepticus*

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The ring chromosome 20 [r (20)] syndrome is a rare syndrome [1]. The first report was described by Atkins, et al in 1972 and approximately 60 cases have been reported in the world[1-3]. The patients have a history of intractable seizure, non-convulsive status epilepticus, behavioral disorder and mild-moderate mental retardation. These symptoms indicate epileptic encephalopathy that is resistant to antiepileptic drugs[4,5]. Unknown pathogenic mechanisms are found with underlying seizure[6,7]. The authors report a rare case of r (20) syndrome associated with epileptic encephalopathy at Queen Sirikit National Institute of Child Health (QSNICH). Thus far, there have also been 2 similar cases reported in Thai adults from King Chulalongkorn Memorial Hospital[8].

Case Report

An 11-year old female patient presented with epilepsy and mild mental retardation for 5 years with no dysmorphic features. On the WISC: III, she scored an IQ of 73 (verbal IQ 67; performance IQ 83). In general, the patient was healthy and there was no family history of consanguineous marriage. Her mother's pregnancy was apparently normal. She was born by cesarean section because of fetal distress. Her birth weight was 2,500 gm. No one in the family had similar symptoms as the patient. When the patient was 6 years old, she had refractory seizures two times at night with a confusion appearance, eye rolling up, left sided head turning and stiffness. The first routine EEG showed within normal limit in awake state with hyperventilation and photic stimulation. She had seizures refractory to pharmacotherapy for 5 years. At 11 years old, she presented with progressive emotion liability, aphasia, a lot of screaming and generalized tonic seizure for 1 month and was diagnosed as non-convulsive status epilepticus (NCSE). During the admission to QSNICH for 2 months, no physical or neurological abnormalities were found. The video-EEG monitoring showed almost continuous bilateral frontal slow-wave and epileptiform discharges over the bilateral frontal regions with refractory electrographic seizures with altered consciousness, agitation, laughter, aggression, staring and hallucination. Examples of video-EEG monitoring were shown in Fig. 1 and 2.

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The brain MRI performed showed focal cortical dysplasia along the medial left inferior temporal gyrus and generalized brain atrophy (Fig. 4). Cytogenetic studies showed mos 46, XX, r (20) (p13q13.3) [17]/46, XX) [43] (Fig. 5).

The patient was treated with several antiepileptic drugs including carbamazepine, valproic acid, clonazepam, phenytoin, vigabatrin, phenobarbital, leviteracetam, cobazam, lamotrigine and zonisamide. Seizures were poorly controlled. The patient became aphasic and up to 12 mcg/kg/min intravenous midazolam was administrated along with other antiepileptic drugs such as leviteracetam, cobazam, zonisamide and lamotrigine. Midazolam was finally tapered off. After this treatment, her clinical status showed an improvement when compared with her previous condition. The video-EEG monitoring is displayed in Fig. 3.

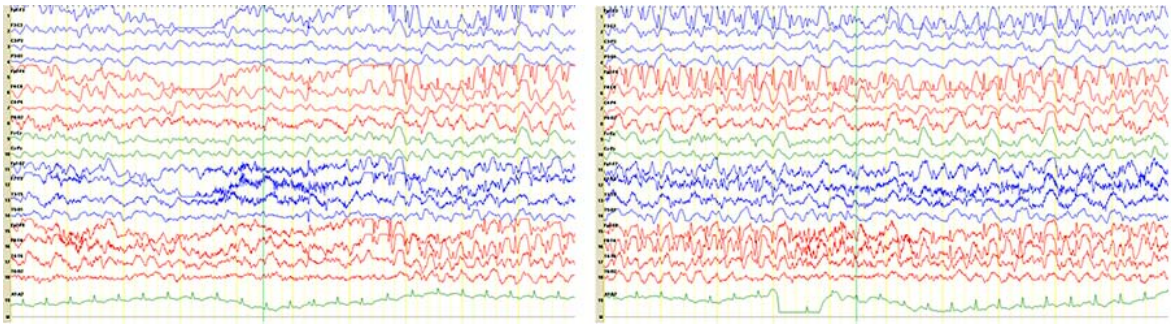

Fig. 1 Ictal EEG. The patient was staring and no responded. The EEG showed run of spike-wave discharges over the bilateral frontal regions. The duration was approximately 15-20 seconds.

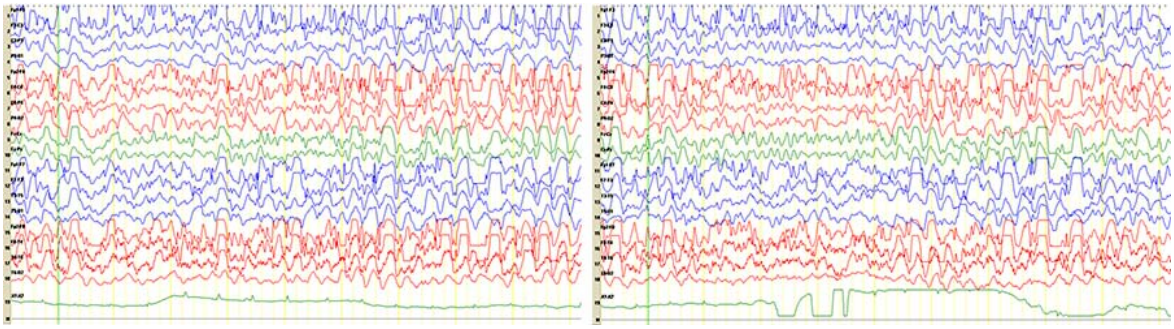

Fig. 2 Ictal EEG. The patient was staring and moving the left arm with no response. The EEG showed run of spike-wave discharges over the bilateral frontal regions intermixed with generalized background slowing.

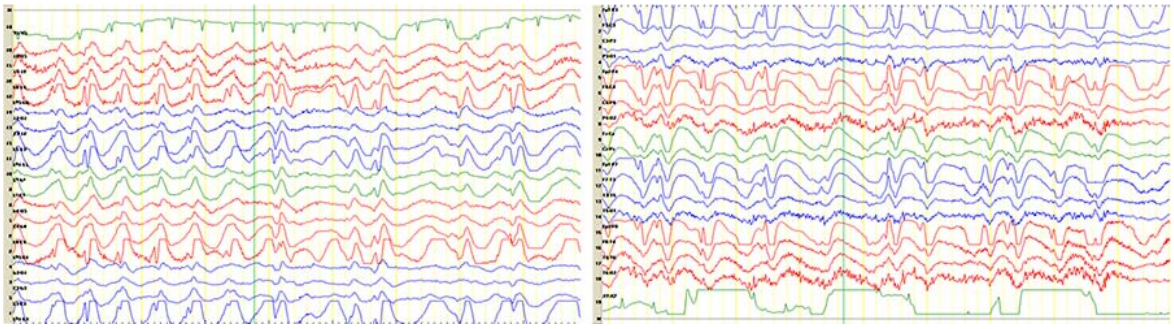

Fig. 3 The general background was present generalized high amplitude delta activities and slow bilateral frontal spike-wave discharges. The patient could talk and draw a picture.

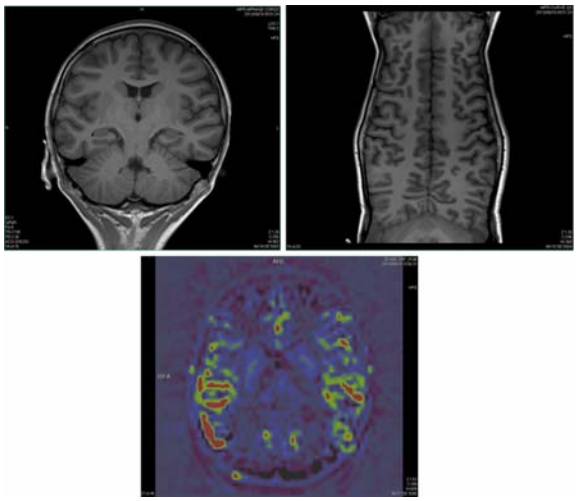

Fig. 4 Brain MRI showed focal cortical dysplasia in medial left inferior temporal gyrus.

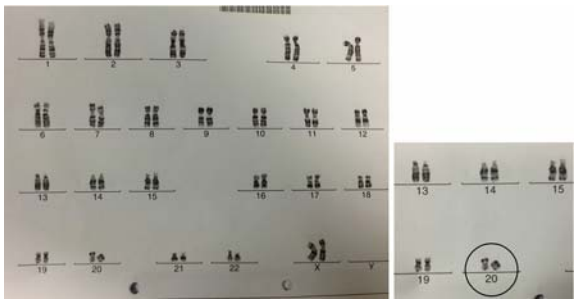

Fig. 5 The patient's chromosome: mos 46, XX, r (20) (p13q13.3) [17]/46, XX) [43].

Discussion

The authors report a patient with r (20) syndrome presenting with prolonged refractory epilepsy, which was resistant to drug therapy and cognitive deterioration with NCSE. The electrographic seizures were confirmed by the continuous video-EEG monitoring. Her condition improved upon treatment with titrated intravenous midazolam and other antiepileptic drugs.

The previous study demonstrated that seizure onset occurred between 6 months and 17 years of age[4]. Seizures are usually complex, partial seizures and characterized as episodes of alteration of consciousness with staring, oral automatisms, bizarre behaviors, hallucination, focal motor seizures and/or head turning[3,4,6,8]. One case was recently reported with Gelastic seizures in r (20) syndrome[9]. Patients with r (20) syndrome usually have a period of prolonged confusion for several minutes to hours are described as drug resistant NCSE. These prolonged seizure episodes with subtle bizarre behavior appear to be a specific seizure pattern in r (20) syndrome. Nocturnal seizures are frequently seen in r (20) syndrome with features of frontal lobe epilepsy, which often go unrecognized, and thus may require further investigation[3,4,6,10].

In the present study, the patient had mild mental retardation. Uncontrolled seizure activities may aggravate learning disabilities and other behavioral problems such as aggression, hyperactivity and attention deficit. Many antiepileptic drugs are also associated with behavioral problems. However, previous studies have reported r (20) syndrome associated with mental retardation and behavioral problems[3-6].

The EEG abnormalities have a wide spectrum. They have been described as mostly bifrontal spike/sharp wave discharges enhanced by sleep state and diffuse generalized background slowing when patients have series of prolonged seizure with diffuse slowing intermixed with a run of bifrontal spike-wave complexes[1,3,4,10,11]. The EEG of this patient is similar to previous studies. However, the video-EEG recording cannot differentiate r (20) syndrome from other refractory epilepsies. Additional history and clinical correlation are needed for diagnosis. Interictal discharges predominantly present in the sleep state can be seen in other epileptic encephalopathies such as Lennox-Gastuat syndrome (LGS), epileptic status epilepticus of sleep (ESES) and Landau-Kleffner syndrome[3,6]. Ictal and Interictal EEG abnormalities in r (20) are sometimes difficult to distinguish and probably require clinical correlation with video monitoring[3,4].

The majority of patients with r (20) have no structural abnormalities demonstrated by neuroimaging. However, minor structural abnormalities have been reported in few patients[4-6]. This patient had focal cortical dysplasia along the medial left inferior temporal gyrus and generalized brain atrophy without EEG correlation.

Conclusion

The patients with r (20) syndrome usually have frequent, prolonged and intractable seizures resistant to antiepileptic medications. They may also have mental retardation, behavioral problems and require multiple antiepileptic drug treatment. The video-EEG monitoring often shows patterns of frontal lobe seizures while neuroimaging usually shows no major abnormalities.

Potential conflicts of interest

None.

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Ring chromosome 20 กลุ่มอาการโรคลมชักที่พบน้อย: รายงานผู้ป่วย 1 รายของสถาบันสุขภาพเด็กแห่งชาติมหาราชินี

ธนินทร์ เวชชาภินันท์, สมจิต ศรีอุดมขจร, ศิโรรัตน์ สุวรรณโชติ

รายงานอาการทางคลินิก, ผลการตรวจคลื่นไฟฟ้าสมอง, ภาพถ่ายเอกซเรย์สมอง (MRI), และผลตรวจโครโมโซมของผู้ป่วยเด็กหญิงพบว่ามีความผิดปกติของโครโมโซม 46, XX, r (20) (p13q13.3) ซึ่งเป็นความผิดปกติที่พบน้อยมาก ผู้ป่วยมีระดับสติปัญญาต่ำเล็กน้อย, อารมณ์เปลี่ยนแปลงง่าย, และมีอาการชักที่ควบคุมยาก ร่วมกับอาการชักต่อเนื่องชนิดไม่มีอาการภายนอก ทำให้ผู้ป่วยดูสับสนร่วมกับมีหรือไม่มีอาการทางการเคลื่อนไหว ภาพถ่ายเอกซเรย์สมองพบความผิดปกติเป็น focal cerebral dysplasia ที่ตำแหน่ง temporal ด้านซ้ายได้มีการติดตามการรักษาโดยใช้การตรวจคลื่นไฟฟ้าสมองอย่างต่อเนื่องพบคลื่นไฟฟ้าลมชักที่ตำแหน่งทางด้านหน้า อาการผู้ป่วยดีขึ้นหลังได้รับยา midazolam ชนิดเข้าเส้นเลือดแบบต่อเนื่อง

ผู้ป่วยโรคที่ลมชักที่ควบคุมได้ยาก ระดับสติปัญญาต่ำ พฤติกรรมเปลี่ยนแปลง ไม่มีลักษณะความผิดปกติ ภายนอกร่วมกับพบคลื่นไฟฟ้าลมชักที่ตำแหน่งทางด้านหน้า ควรคิดถึงภาวะโครโมโซมผิดปกติโดยเฉพาะโครโมโซมวงแหวนคู่ที่ 20
