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Case Report

Refractory and severe status epilepticus in a patient with ring chromosome 20 syndrome

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Abstract

Ring chromosome 20 [r(20)] syndrome is a rare chromosomal disorder that is characterized by the development of refractory epilepsy during childhood with gradual declines in cognitive performance and behavior. Although the prognoses of seizures and intellectual disability associated with this condition are poor, life-threatening complications have rarely been described. We herein presented a case of a 17-year-old female with [r(20)] syndrome who developed recurrent status epilepticus (SE) at 14 years of age that evolved into unremitting SE in spite of vigorous antiepileptic treatments. She was administered thiopental anesthesia for 1 year, and was subsequently left in severe neurological sequelae. It is important to note that patients with this syndrome not only have severe epileptic encephalopathy persisting into adulthood, but are also at risk of fatal SE.

Keywords: Ring chromosome 20 syndrome; Epilepsy; Status epilepticus; Sodium thiopental anesthesia

1. Introduction

Ring chromosome 20 [r(20)] syndrome, initially reported by Atkins et al. in 1972, has since been characterized by childhood-onset refractory epilepsy, mild-to-moderate mental retardation, and the lack of recognizable dysmorphic features despite a well-defined chromosomal disorder [1,2]. Normal development prior to the onset of seizures is common; therefore, difficulties are associated with making a diagnosis even after the onset of epilepsy. Seizures are frequent and refractory to medications, resulting in gradual declines in cognitive performance and behavior. In the long-term prognosis of this condition, patients continue to have seizures and eventually develop moderate to severe mental retardation; however, fatal or serious complications have rarely been described. Jacob et al. first reported a child with [r(20)] syndrome with a catastrophic clinical course [3]. We herein presented a second case of a female who exhibited bouts of SE that evolved into unremitting SE, and was left in severe neurological sequelae.

2. Patient presentation

The patient was a 17-year-old Japanese girl born to unrelated healthy parents at 39 weeks of gestation. The delivery was uncomplicated and the birth weight was 2900 g. Her family history was negative for seizures, although her old brother had a previous history of febrile seizures. She achieved normal psychomotor development until 7 years of age, at which time she developed epileptic seizures that were characterized by the loss of consciousness for 1 or 2 min. She was diagnosed with cryptogenic frontal lobe epilepsy and the administration

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of carbamazepine (CBZ) was initiated at a local hospital. Difficulties were associated with increasing the dose of CBZ due to the side effect of sleepiness. Therefore, CBZ was switched to valproate acid (VPA), which also failed to decrease the daily frequency of seizures. At 9 years of age, she was referred to another hospital, and received an intensive anticonvulsant drug (AED) treatment for 1 year without success. She was found to be very sensitive to dose-related AED [VPA, CBZ, zonisamide, clobazam, phenytoin, and phenobarbital (PB)] side effects such as sleepiness, malaise, and a character change, and, thus, it was difficult to increase the serum concentrations of AED to therapeutic ranges (Fig. 1). At 11 years of age, she was referred to our hospital because her family had moved home.

In initial examinations, her neurological and physical examinations were negative, except for slow speech and mild ataxia. There were no dysmorphic features in the face or extremities. Interictal routine EEG showed frequent intermittent runs of diffuse rhythmic spike-and-wave activities at 2–2.5 Hz with bifrontal predominance (Fig. 2A). Long-term EEG monitoring captured several focal tonic vibrating seizures that lasted a few minutes and arose electroencephalographically from both frontal regions. Two other types of epileptic seizures were also recorded: (1) prolonged atypical absence seizures corresponding to runs of diffuse spike-and-wave complexes, and (2) focal seizures with terror and impaired consciousness during sleep, arising from both frontal regions.

Brain MRI showed a normal appearance. Interictal ^{123}I-iomazenil (IMZ)-SPECT revealed the decreased uptake of IMZ in both frontal regions. The WISC-III test showed a full scale IQ of 45 (VIQ = 56, PIQ = 44). The characteristic EEG pattern, refractory clinical course, and cryptogenic etiology suggested [r(20)] syndrome. Karyotyping revealed 46,XX,r(20)(p13q13.3)[23]/45,XX,-20[1]/46,XX[6] and this chromosomal abnormality was detected in 76% of the lymphocytes tested.

Focal tonic vibrating seizures occurred exclusively during sleep, up to 10 times every night. We administered various AEDs and also a classic 4:1 ketogenic diet without any effects. Thus, AED treatments had to be maintained with relatively low VPA and CBZ doses. After 12 years of age, she developed episodic bouts of focal tonic vibrating seizures, requiring brief admissions for the intravenous administration of midazolam or phenytoin. At 13 years of age, the number of seizures increased to every 10 min, and finally evolved into unremitting tonic SE, refractory to intravenous midazolam, phenytoin, and high-dose phenobarbital. Finally, we introduced sodium thiopental (STP) anesthesia under artificial respiration. STP was given with an initial bolus injection of 3 mg/kg, followed by continuous infusion of 2 –5 mg/kg/h to maintain the burst-suppression EEG pattern. However, the tonic SE became uncontrollable whenever we tried to reduce STP dose and withdraw from the anesthesia (Fig. 2B). STP anesthesia had to be maintained for nearly 1 year under artificial respiration with tracheotomy and gastrostomy. Thereafter, recurrences of the tonic SE gradually decreased in frequency despite the gradual reduction of STP dose. She was eventually weaned off from STP at 15 years of age,

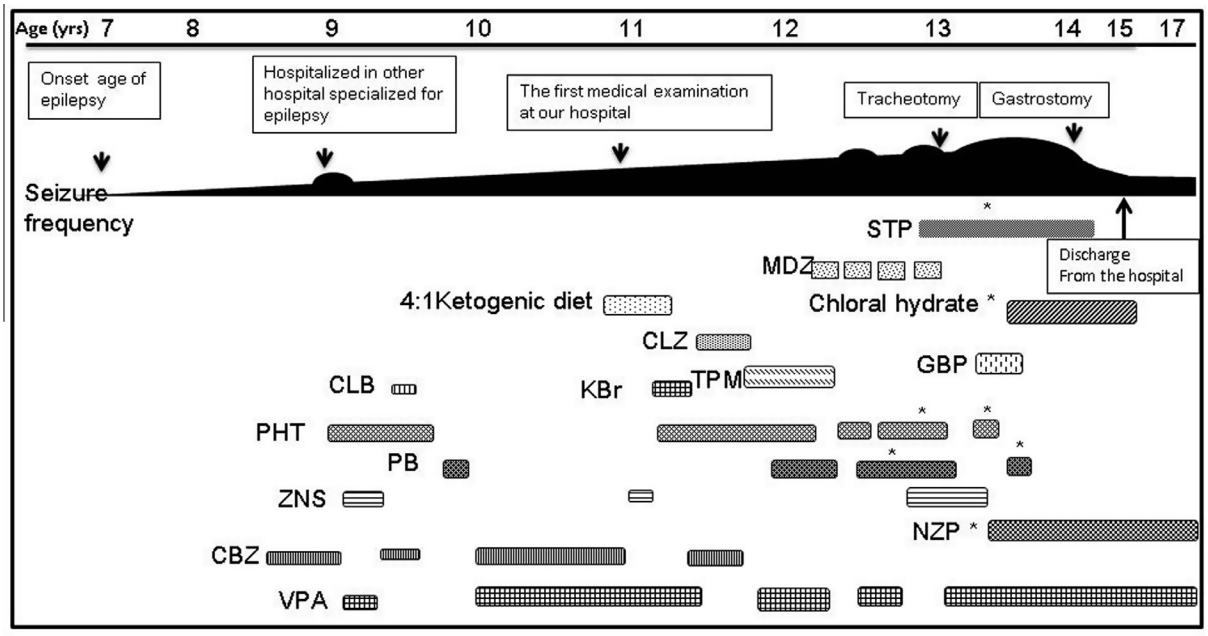

Fig. 1. Clinical course of our patient. None of the available antiepileptic drugs or classical 4:1 ketogenic diet therapy controlled recurrent SE. *Abbreviations:* STP: sodium thiopental, MDZ: midazolam, VPA: valpropic acid, CBZ: carbamazepine, PHT: phenytoin, PB: phenobarbital, ZNS: zonisamide, NTZ: nitrazepam, CLB: clobazam, TPM: topiramate, GBP: gabapentin, KBr: potassium bromide, CLZ: clorazepate, *: high-dose trial.