PARTIAL EPILEPSY AND DEVELOPMENTAL DELAY IN INFANT WITH RING CHROMOSOME 14

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Summary: *Partial epilepsy and developmental delay in infant with ring chromosome 14:* Ring chromosome 14 (r14) is clinically characterized by early-onset epilepsy, mental retardation, delayed speech, microcephaly, extremely mild facial dysmorphisms and ophthalmologic abnormalities. We report a case presenting with partial seizures and delayed development in infancy in which r14 was diagnosed based on chromosomal analysis. The patient was a girl with a normal family and delivery history. Afebrile generalized convulsions developed at age 9 months, and phenobarbital was started, but was changed to zonisamide due to impaired liver function. Chromosome analysis led to a diagnosis of 46, XX, r(14) (p11.2q32.3). At age 5 years, while under treatment with zonisamide and clobazam, epilepsy was characterized by multiple daily episodes of complex partial seizures. Although there are no consistent brain MRI or electroencephalogram findings, experienced pediatric neurologists can make a diagnosis based on facial dysmorphisms. When refractory epilepsy is encountered in infancy with developmental delay of unknown cause, chromosome analysis should be performed.

Key-words: Chromosomal abnormality – Seizure – Convulsion.

INTRODUCTION

Ring chromosome 14 (r14) is a rare epilepsy syndrome, the phenotype of which was defined by Rethore *et al.* in 1984 (4). It is clinically characterized by early-onset epilepsy, mental retardation, delayed speech, microcephaly, extremely mild facial dysmorphisms, and ophthalmologic abnormalities (1). We report herein a case of a girl who presented with partial seizures and delayed development in infancy and was diagnosed with r14 based on chromosomal analysis.

CASE REPORT

The patient is a girl with normal family history and delivery history. Motor development: At 3 months of age, the patient developed social smile, with stable head and neck control, and she could roll over at 6 months of age. Facial features were characterized by blepharophimosis, flat nose, and almond-shaped eyes. Afebrile generalized con-

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vulsions developed at 9 months of age, and the patient was started on phenobarbital. Phenobarbital treatment resulted in impaired liver function, and the medication was switched to zonisamide. Partial seizures frequently occurred thereafter but were temporarily controlled with the addition of clobazam 0.8 mg/kg/day to zonisamide 9 mg/kg/day. This was a case of partial epilepsy with delayed development and facial abnormalities which had developed in infancy, and g band chromosome analysis led to a diagnosis of 46, XX, r(14) (p11.2q32.3) (Fig. 1). Head circumference at the age of 2 years and 7 months was 44.5 cm (-2.3 SD). The child has been in physical therapy since the age of three, and has learned to walk. She began speaking at the age of 4 years. Background activity on sleep electroencephalogram at the age of 4 years showed a predominance of 12 to 16 Hz waves, and the development of high-amplitude slow waves with spikes. The spikes developed in the left and right occipital, right central, and left temporal regions, and were often multifocal. Brain MRI was normal. At the age of 5 years, while being treated with zonisamide 10 mg/kg/day and clobazam 1.0 mg/kg/day, the patient's epilepsy was characterized by multiple daily episodes of complex partial seizures, with no generalized seizures.

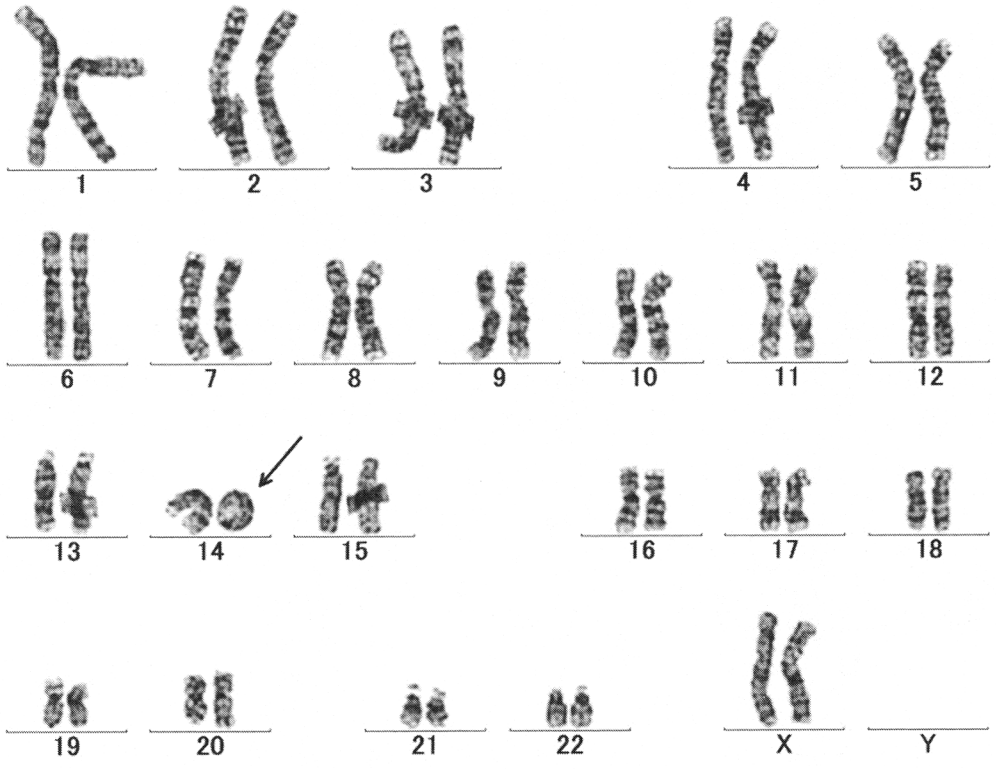

Figure 1: Cytogenic investigation of the patient showed 46, XX, r(14) (p11.2q32.3).

DISCUSSION

Ring chromosome 20 syndrome is known as a form of refractory epilepsy, while r14 is rarely reported. Mental retardation and epilepsy have been described in all previously reported cases of r14 (1-6). Ring chromosome 14 is known to involve various types of seizures, and is not associated with any characteristic type of seizure. In r14, seizures are often poorly controlled, despite treatment with two or more antiepileptic medications (5). In addition to epileptic seizures, psychomotor retardation develops in early childhood (2). No consistent brain MRI or electroencephalogram findings have been reported. Experienced pediatric neurologists can make a diagnosis based on facial dysmorphisms, but it appears that this syndrome is often overlooked as merely refractory epilepsy developing with mental retardation in infancy. Nevertheless, a review of the occasional reports in the past suggests that r14 epilepsy is characterized by early development (1-6). The initial epileptic seizure occurred before 10 months of age in most reported cases (3, 6). When refractory partial epilepsy is encountered in infancy with developmental delay of unknown cause, it is important for clinicians involved in the field of epilepsy to perform chromosome analysis with r14 in mind.

REFERENCES

1. *DE BLOIS M.C., CAILLE B., RETHORE M.O., DUFIER J.L., LEJEUNE J.:* r14 syndrome without major dysmorphism. *Ann. Genet.,* 1990, *33*, 155-158.
2. *FRENNY J.S., NILANG S.:* Ring chromosome 14 with epilepsy and developmental delay. *Indian Pediatrics,* 2006, *43*, 744-745.
3. *MORIMOTO M., USUKU T., TANAKA M., OTABE O., NISHIMURA A., OCHI M., TAKEUCHI Y., YOSHIDA H., SUGIMOTO T.:* Ring chromosome 14 with localization-related epilepsy: three cases. *Epilepsia,* 2003, *44*, 1245-1249.
4. *RETHORE M.O., CAILLE B., HUET DE BAROCHEZ Y., DE BLOIS M.C., RAVEL A., LEJEUNE J.:* Ring chromosome 14. II. A case report of r(14) mosaicism. The r(14) phenotype. *Ann. Genet.,* 1984, *27*, 91-95.
5. *SCHIADE B.K., COSTA T., SUMMERS A.M., NOWAEZYK M.J., COX D.W.*: FISH mapping of telomeric 14q32 deletions: search for the cause of seizures. *Am. J. Med. Genet.,* 2005, *138A*, 218-224.
6. *VILLE D., DE BELLESCIZE J., NGUYEN M.A., TEATARD H., GAUTIER A., PERRIER J., TILL M., DES PORTES V.:* Ring 14 chromosome presenting as early-onset isolated partial epilepsy. *Dev. Med. Child. Neurol.,* 2009, *51*, 917-922.

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