14q32.33 Deletion Identified by array-CGH in a 5-year-old-girl with Seizure

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Deletions of 14q including band 14q32.33 are uncommon. Patients with terminal deletions of chromosome 14 usually share a number of clinical features. By molecular techniques (array comparative genomic hybridization (CGH) and fluorescence in situ hybridization (FISH), we identified a young girl with 0.3 Mb terminal 14q32.33 deletion. Review of the nine cases with pure terminal 14q32.3 deletions described to date documented that our observation is the smallest terminal 14q deletion ever reported. The phenotype of our patient is much less severe than the phenotypes of the patients reported previously. We report our experience in examining the clinical, behavioral, and cognitive findings in a 5-year-old girl studied with chromosomal microarray hybridization and reviewed previously reported patients with 14q32 deletions.

Key Words: 14q32.33 deletion, Fluorescence in situ hybridization, Array comparative genomic hybridization

Introduction

Terminal deletions of the 14q32.3 sub-band of the long arm of chromosome 14 are rare¹. The common clinical features shared by a significant number of patients with 14qter deletions include microcephaly, high forehead with lateral hypertrichosis, broad nasal bridge, long and broad philtrum, high arched palate, epicanthic folds, single palmar crease, hypotonia, and mild to moderate mental retardation and developmental delay¹,². The phenotypic variation may occur as a result of a slightly different deletion breakpoint. Due to the limited number of cases reported, it was not possible to assign specific features to specific regions of terminal 14q³.

Here, we report on a girl with a small sub–telomeric deletion of the long arm of chromosome 14q32.33 (smaller than previously described) and compare her phenotype with previously reported patients with similar 14q deletions, due to either a linear deletion or a ring chromosome 14.

Case report

The proband, a Korean 5-year-old-girl, is the second child of healthy unrelated parents. The girl was delivered at 38 weeks after an uneventful pregnancy. Familial
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DISCUSSION

The focus of our report was to describe an additional patient with a deletion involving the 14q32 band and to review the literature. A purely distal 14q32 deletion was reported in less than 15 published cases[^4], and only 12 of them were confirmed by molecular cytogenetics. Nine patients bearing 14q32.3 terminal deletion have been reported to date. Deletions involving exclusively band 14q32.3 have thus far been observed in the rare terminal deletions of 14q and in carriers of a ring
Fig. 2. Array CGH showing a deletion on the long arm of chromosome 14 (14q32.3 region). The arrow indicates a deletion at chromosome 14q32.33→qter.

Fig. 3. FISH with 14q32.1 (green color) and 14q32.33 (yellow color) region probes; the arrow indicates a deletion of the probe (Wi-6905-) in a del(14)(q32.33) chromosome.

chromosome 14q. Major clinical features are mental retardation and dysmorphism. Major congenital malformations are relatively uncommon in terminal 14q deletion patients, except for congenital heart defects. The following list of commonly observed physical anomalies reported in patients with the 14q32.3 deletion: broad philtrum (6/6), broad and flat nasal bridge (5/6), telecanthus (6/8), hypotonia (5/8), high-arched palate (6/8), thin upper lip (4/5), blepharophimosis (5/6), pointed chin (3/7), malformed helices (3/5), small mouth (3/6), and strabismus (3/6). This suggests that genes involved in the clinical features classically reported in 14q32.3 deletions could be located on the telomeric 1–1.6 Mb of the 14q32.33 terminal sub-band of chromosome 14q. Our patient did not display all abnormalities that are commonly found in the terminal deletion cases including broad and long philtrum, high arched palate, telecanthus, blepharophimosis, and thin upper lip. Our patient has a terminal deletion (0.3 Mb) shorter than those previously published. This phenotypic variation may be the result of a slightly different deletion breakpoint. The general phenotype of cases with terminal 14q deletion due to ring chromosome is similar or less severely affected than that of cases with linear chromosome deletions of similar size. Specifically, growth retardation is less frequently associated with ring chromosome 14 cases. Seizures and retinitis pigmentosa are not found in patients with linear terminal 14q deletions, but only in 14qter deletions due to ring chromosomes. Interestingly, our patient has a seizure disorder, and it is not commonly found in other reported cases. The literature review reveals only one case report of seizure of the patients with 14q32.3 deletion. These findings should contribute to delineate the emerging phenotype in terminal 14q32.3 deletion but further data will be necessary. The clinical features including cognitive and behavioral findings of the twelve terminal 14q32 deletion cases and of this case are listed in Table 1. Considering that our patient’s major clinical feature is mental retardation and seizure, we focused our attention on neurologically implicated genes in terminal 14q32.33 deletion. In this region, two genes BX248748 and MTA1 have a putative role in neurolo-
gical development\(^1\). Regulation of genes proximal to the deletion such as JAG2, AKT1, and CKB may also be associated\(^1\). Considering these reports, several candidate genes could be involved in the development of the mental retardation and seizures observed in our patient. But molecular genetic and functional studies are required to elucidate the contribution of each gene to a specific phenotype. High resolution techniques, such as chromosome microarray hybridization, allows for a more precise description of location, size, and genes involved in a specific chromosome region, and are helpful to characterize the genetic locus for genotype–phenotype correlations\(^3\). Thus, the natural history and genetic background need to be further investigated in order to provide appropriate management and genetic counseling.

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References