RECURRENT UNBALANCED CONSTITUTIONAL CHROMOSOMAL TRANSLOCATION BETWEEN CHROMOSOMES 8 AND 12, DER(8;12)(P23.1;P13.31), DETECTED IN THREE PATIENTS WITH SIMILAR PHENOTYPE

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Background

Recurrent constitutional reciprocal non-Robertsonian chromosome translocations are rare. To our knowledge, there are only three such balanced translocations reported in the literature; the most common one is t(11;22) (q23;q11), while t(8;22) (q24.13;p11.21) and t(4;8)p16;p23 are less frequently seen. Recurrent unbalanced translocations, most notably der(4)(4;11)(p16.2;p15.4), have been also reported. Here we report an apparently recurrent unbalanced translocation between the short arms of chromosomes 8 and 12 [der(8;12)(p23.1;p13.31)] found in three cases referred to our clinical diagnostic laboratory for chromosomal microarray (CMA).

Methods

• These three blood specimens were sent to our clinical genetics laboratory between August 2014 and May 2017 for CMA and were tested by a custom-designed 180K genome array with SNP (Agilent). During this time, total 14,607 whole genome microarray studies were performed.

• Parental testing was performed by fluorescence in situ hybridization (FISH) using probes from within the deleted and duplicated regions (Empire Genomics) on two of the three families; the third family was not available for FISH testing.

• Phenotypic information was available on two of the probands and compared to the three cases reported in the literature.

Results

• CMA revealed a ~7 Mb terminal deletion at 8p23.2p23.3 and a concomitant ~8.3 Mb terminal duplication of 12p13.33p13.31 in three probands (see Figure 1).

• Metaphase FISH using probes from within the deleted and duplicated regions performed on two probands showed that these aberrations were secondary to a derivative chromosome 8, der(8)t(8;12)(p23.1;p13.31) (see Figure 2A).

• Metaphase FISH on parental blood in two of the families revealed a normal hybridization, consistent with a de novo occurrence of the unbalanced translocation in the probands (see Figure 2B).

Conclusions

Only three patients with a similar derivative chromosome 8 [der(8)t(8;12)(p23.1;p13.31)] resulting in terminal deletions and duplication of 8p and 12p, respectively, have been reported in the literature previously to our knowledge. We identified an additional three such patients with the same derivative chromosome (0.09%) from 14,607 consecutive CMA cases. Parental FISH studies on two of our patients and one reported in the literature showed no predisposing balanced rearrangement, consistent with the de novo origin in all cases in which inheritance has been studied. The 8p23.1 and 12p13.31 chromosome regions are known to contain highly homologous low-copy repeat (LCR) clusters which may predispose them to rearrangement.

In summary, the der(8)t(8;12) appears to be a recurrent de novo unbalanced translocation mediated by large LCRs and associated with the phenotype of developmental delay, hypotonia, childhood onset epilepsy, and autistic features.

References