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CLINICAL AND IMMUNOLOGICAL EVALUATION OF FIVE PATIENTS WITH ATYPICAL 22q11.2 DELETION SYNDROME

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Background:

The peculiarity of the 22q11.2 deletion syndrome is the great phenotypic heterogeneity making it a classic example of a syndrome with variable expressivity and incomplete penetrance. The reasons for this variability have not been completely elucidated. Deletions in 22q11.2 region are a consequence of non-allelic homologous recombination (NAHR) due to misalignment of low copy repeats (LCRs) during meiosis. Eight LCRs (named LRC22-A to H) have been identified, but only the four centromeric ones (LCR22-A to D) are implicated in this syndrome. As known, 90% of patients share a 'classic' ~3Mb deletion between LCR22-A and LCR22-D.

Methods:

We analyzed a cohort of 23 patients, focusing on the genetic and immunological data of 5 cases with atypical deletions.

Results:

In one case the deletion was mediated by LCR-A and B, whereas in the other 4 cases the mechanism of deletion seems not to be mediated by a NAHR event. Analysis of the additional Copy Number Variations (CNVs) elsewhere in the genome was also performed. Two rare CNVs were detected in one patient, and their gene content could influence the phenotype.
Physical examination revealed a wide heterogeneity; however, global developmental delay and/or mild mental retardation, more prominent in language, was found in all patients and autistic traits in two. None of them had cardiac malformations. An "extended" immunophenotype revealed a severe T cell immunodeficiency in all patients, particularly in CD8+ subset, and in both naïve and recent thymic emigrants subsets.

Conclusions:

The variable extension of the deleted region could be a cause underlying the phenotypic heterogeneity.