Partial trisomy 19p13 is associated with a novel syndrome of immunodeficiency, psychomotor retardation, facial dysmorphia, and urogenital malformation

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Case Report: We recently reported on a 7 year-old boy with partial trisomy 19p13 [46,XY.ish dup(19(pterÆp13.2)t(15p;19p)de novo] showing a syndromic disorder associated with immunodeficiency. This boy had been born prematurely in the 32nd week of gestation whereupon the growth-restricted infant presented with profound motor and mental retardation, epilepsy, facial dysmorphia and perineal hypospadia. Meanwhile, another 2 year-old patient was identified, born prematurely at 31+1 weeks of gestational age (660g; 34cm; 23.5cm) with urogenital malformations (horseshoe kidney, hypospadia), microcephalus, flat nasal bridge, telecanthus, short upslanting palpebral fissures, long eyelashes, strabismus, hypermetropia, long philtrum, narrow/thin lips, micrognathia and pharyngeal instability.

Results: Patient 2 has a comparable chromosomal duplication like patient 1 [arr cgh 19p13.3dup] and an additional aberration on chromosome 16 [46,XY.ish der(16)t(16;19)(p13.3;p13.3)], involving the alpha-hemoglobin locus (16p) and resulting in alpha thalassemia minor/intermedia. Both patients share most syndromal features and immunologic abnormalities. With respect to the immunodeficiency, both show recurrent invasive bacterial infections, including pneumonia, recurring bronchitis and otitis. Immunological tests found no alterations in global T-, B-, nor NK-cell counts, nor lymphocytic proliferation, but almost absent class-switched B memory cells in the second patient and reduced NK cytotoxicity in both. Immunoglobulin analysis revealed selective antibody deficiency against polysaccharide antigens in one and reduced IgG1, -3 subclass levels as well as an IgM deficiency in the other boy. In both patients granulocytic oxidative burst assays demonstrated a moderate and borderline reduction, respectively, whereas monocytic respiratory burst was decreased in both. Additionally, patient 1 has a reduction and patient 2 a complete lack of mannan-binding lectin. In both boys, regular immunoglobulin substitution significantly decreased the number and severity of infections and led to improved thriving.

Conclusions: Although symptoms in patient 2 in part resemble alpha-thalassemia/mental retardation syndrome (ATR-16, OMIM #141750; 16pter-p13.3) and might occur independently of trisomy 19p13, the similar set of findings in two independent patients with a very similar chromosomal abnormality, especially with regard to the immunological phenotype, suggests that subtelomeric partial trisomy 19p leads to a complex syndromic disorder with immunodeficiency. Further analyses will need to determine the molecular origin of B lymphocyte and granulocyte abnormalities.