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Laboratory Medicine 2018: IgG4 deficiency with gene deletion in down syndrome: Lynn Cintron1: Jeraiby M 1, Lambert C2

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Background & Aim: IgG4 deficiency is more frequent among persons with Down syndrome (DS), without identifying explanation. The role of IgG4 deficiency which is not fully established for many affected persons in the general population are asymptomatic. Nevertheless, in the context of DS it may be an important factor in repeated infections and even stroke. The aim of the present study was to investigate the molecular mechanism of IgG4 deficiency at the level of the heavy chain gene (IGHG4) gene. Methodology: Quantitative real-time polymerase chain reaction (Q-PCR) was carried out to measure IGHG4 copies number with SYBR Green detection and comparison to a reference gene (36B4). A IGHG4/36B4 ratio was considered normal (2 copies of IGHG4) when between 0.8 and 1.2. We studied 44 DS persons: 21 males and 23 females from 7 years to 57 years, composed of 23 DS persons (11 males and 12 females) carrying severe IgG4 deficiency (<0.02 g /L), 5 having an IgG4 level not detectable and 21 DS subjects (10 males and 11 females) with no IgG4 deficiency (level >0.1 g /L). The patient group was compared with 38 healthy donors (controls) without DS. Results: IGHG4 heterozygous deletion was found in 16 (69.6%) DS patients with IgG4 deficiency versus in 2 (9.5%) DS subjects without IgG4 deficiency (p=0.0001 with Yates correction) in the control group, no deletion was seen. Conclusions: IGHG4 haploinsufficiency is highly correlated to IgG4 deficiency in our population with DS, but other factors exist that needs to be identified. We report four children with Down Syndrome (DS) without evidence of congenital heart disease who sustained cerebral infarction in the context of an infectious disease. In one child, stroke occurred in the context of acute infection with Mycoplasma pneumonia. In another child, stroke occurred in the context of Streptococcus oralis (viridans subgroup) infection. In two other children, stroke occurred in the context of a bibasilar pneumonia for which an etiologic agent was not found. All patients had evidence of selective IgG4 subclass deficiency. We followed 8 other children with down syndrome with infectious diseases, but without stroke and a control group of healthy children, and measured the value of IgG4 for each group. We found a statistical significant difference of levels of IgG4 subclass deficiency in the group of stroke, in comparison with the other two groups (P values <0.001). We, therefore, suggest an association between IgG4 subclass deficiency and stroke in DS patients. IgG4 subclass deficiency could conceivably play a role in the high frequency of para-infectious related stroke in this population.

Foot Note: This work is partly presented at Joint event of 13th International Conference on Laboratory Medicine & Pathology, June 25-26, 2018 | Berlin, Germany