NEUTROPHIL FUNCTION AND ADAPTIVE IMMUNE SYSTEM ABNORMALITIES IN LAD I AND LAD III DEFICIENT PATIENTS

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Background and aims

Leucocyte adhesion deficiency is rare autosome-recessive disorder, characterized impaired leucocyte migration and severe life-threating infections. LAD-deficiency is usually fatal; few patients survive to adulthood without HSCT.

Methods

We present evaluation of neutrophil function (adhesion molecules expression, migration, respiratory burst) and lymphocytes subsets in 10 patients with genetically-confirmed ***LAD-I (n=7)*** and ***LAD-III (n=3).***

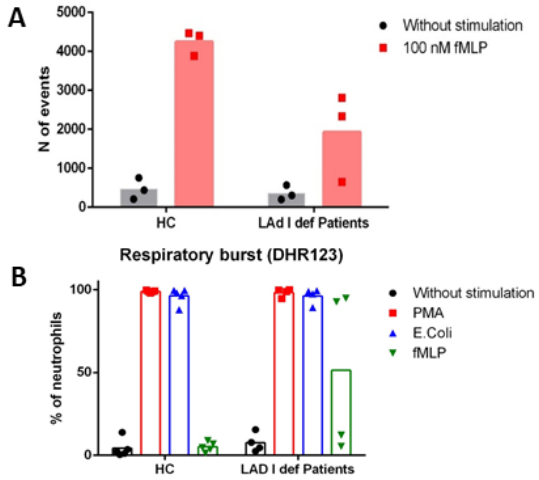
Results

LAD-I-cohort enrolls patients in the age from 12 days - 21 years at the moment of investigation. Three of 7 pts with **complete CD18-deficiency** underwent HSCT and/or died in the first years of life, therefore Immunological tests were restricted and included standard lymphocytes subsets evaluation, revealed only **decreased CD4+-T-cells percentage (p=0.049)**.

Cohort with **partial CD18-deficiency** (9-21 years) includes patients: with CD18-brigh lymphocytes subset (n=2), with "weak" CD18-expression on all leucocytes (n=2). In this cohort neutrophil migration was partially preserved (up to 50% of normal); 2 patients have "hyperactivated" neutrophil phenotype (↓CD62L and ↑CD35-expression) and enhanced "respiratory burst" to fMLP (>90%) (***Figure 1***).

Partial-CD18-deficient patients have **decreased percentage of Naïve-CD4+ T-cells (p=0.0085), RTE (p=0.0001) and Tregs (p=0.0247)** compared to HC (***Figure 2***).

Figure 1. Neutrophil function in patient with partial LAD I -deficiency

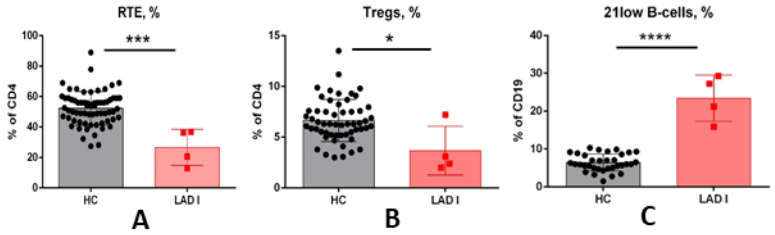


A – evaluation of transwell (3μm pore size) neutrophil migration; B – evaluation respiratory burst (DHR123 staining) to PMA, E. Coli and fMLP.

Both switched and non-switched B-memory cells were variable: from normal-to-elevated (n=2) to decreased-to-absent (n=2). Also **CD21low (p<0.0001, p=0.0068)** and **CD21lowCD38low (p=0.0077, p=0.038) B-cells** percentage and absolute number **were elevated (*Figure 2*)**.

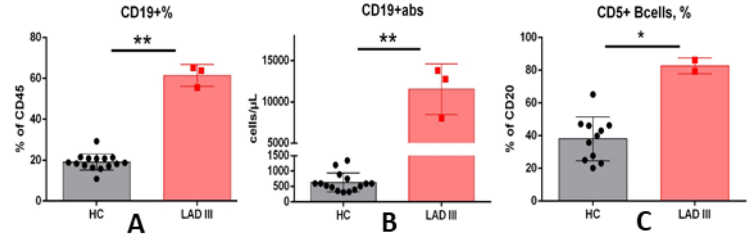
LAD-III deficient cohort includes 3 patients from 2 families (3-6 years, 1pt-died, 2pts- HSCT). In this cohort predominantly **B-cells lymphocytosis** (50-60%of lymph, >12000cells/μL) was noted. Almost all B-cells were **B1** (CD5+, >80%of B-cells) (***Figure 3***).

Figure 2. T-and B-cell abnormalities in patient with partial LAD I -deficiency



A, B and C– percentage of Recent thymic emigrants and Tregs (of CD4+ T-cells) and CD21low B-cells (of B-cells).

Figure 3. B-cell abnormalities in patient with LAD III -deficiency



A and B – percentage and absolute number of B-cells; C – CD5+ B-cell percentage of all B-cell.

Conclusion

Patients with partial LAD-deficiency have sings of immunodysregulation, such as decreased naïve CD4+-T-cells, Tregs, elevated CD21low and CD21lowCD38low B-cells and neutrophils hyperactivation, that can result to increased risks of autoimmune and autoinflammatory complications.

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