

PRIMARY IMMUNODEFICIENCY PRESENTING AS RED BABY SYNDROME

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A 6-month old female infant was referred for scaly erythroderma, failure to thrive, torpid pneumonia and thrush. Erythroderma started at the age of 2 months as a disseminated red maculo-papular rash progressing rapidly to generalized desquamative erythroderma. The differential diagnosis of „red baby syndrome“ includes primary skin diseases (erythrodermia

ichthyosiformis congenita, psoriasis, seborrheic dermatitis, severe atopic dermatitis), immunodeficiency (severe combined immunodeficiency – SCID, complicated by graft-versus-host-disease – GVHD; Omenn syndrome), Netherton syndrome, infectious diseases (neonatal candidiasis, staphylococcal scalded skin syndrome – SSSS), and some metabolic disorders (multiple carboxylase deficiency, disorders of the amino acids). Clear-cut lymphopenia (WBC $5.1 \times 10^9/l$: Ly 31% - absolute count: 1581/l – normal count <2 years: >3000) and severe hypogammaglobulinemia (IgG 1,0 g/l) indicated immunodeficiency. In several determinations a reduced number of T-lymphocytes was found (CD3 7-22%, CD4 5-18%, CD8 4-33%) and invariable complete absence of B-cells (CD19 0%). Genomic analysis demonstrated hypomorphic mutations affecting both alleles of the RAG-1 gene (recombination activating gene, locus 11p13) a pivotal factor in the synthesis and diversification of immunoglobulins and T-cell receptors. Hypomorphic mutations which allow some residual enzyme activity result in a „leaky“ SCID phenotype with a polymorphic or atypical, often severe clinical picture. In this case a reduced number of T-cell clones was being generated with narrowed heterogeneity and strong autoreactivity, resembling the phenotype of GVHD. Skin biopsy was consistent with GVHD, but HLA typing effectively excluded engraftment of foreign T-cells. Leaky phenotype can result from practically all SCID mutations (IL-2R γ c, Artemis, ADA, DNA ligase 4, RMRP, IL-7R α zap70k etc.) if they are hypomorphic. Treatment consists of intravenous immunoglobulin substitution, prophylaxis and treatment of bacterial, CMV, pneumocystis and fungal infections, and emergency hematopoietic stem cell transplantation. The presented infant received a transplant of her father's bone marrow following a myelo- and immunoablative regimen. However, despite initial signs of engraftment, the child died 11 days post-BMT due to profound neutropenia and invasive pulmonary aspergillosis.