

Severe combined immune deficiency, T- B-

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Abstract

Severe combined immune deficiency, [T- B-] is an inherited immune deficiency with autosomal recessive transmission, its incidence is around 1/500,00 births/year. This deficiency occurs in children from the first months of life, and is manifested by recurrent bacterial or viral (cytomegalovirus, Pneumocystis carinii) infections, sometimes BCGitis (if the child received a BCG vaccination during the neonatal period), severe diarrhoea and failure to thrive. SCID can be treated only in a paediatric unit specialized in immunology and haematology. Subjects suspected of having SCID should never be given live vaccines or transfused with non-irradiated blood products. The only treatment of SCID is a bone-marrow transplantation. Several genetic defects can be responsible for SCID of alymphocytosis type. Two genetic anomalies can account for this disorder: either mutation in the recombination-activating (RAG1 and RAG2) genes or in Artemis gene.

Keywords

T-, B- phenotype, bone-marrow transplantation, RAG1 and RAG2 gene, Artemis gene

Name of the disease and synonyms

Severe combined immune deficiency (SCID) / agammaglobulinemia, alymphocytosis type

Diagnostic criteria/definition

This is an inherited immune deficiency with autosomal recessive transmission (MIM: 202500).

Incidence

The incidence of this disease is around 1/500,00 births/year.

Clinical description

This deficiency occurs in infants from the first months of life, manifested by recurrent bacterial or viral (cytomegalovirus, Pneumocystis carinii) infections, sometimes BCG-itis (if the child received BCG vaccinations during the neonatal period), severe diarrhea and failure to thrive (1). The same clinical signs are seen in children with X-linked SCID (MIM: 300400), which accounts for 50% of SCID cases.

Management/treatments

SCID can be treated only in a ward specialized in immunology and hematology. Subjects suspected of having SCID should never be given live vaccines or transfused with non-irradiated blood products. The only treatment of SCID is a bone-marrow transplantation.

Etiology

Several genetic defects can be responsible for SCID, alymphocytosis type. A small number of subjects have a defect in adenosine deaminase (ADA) (MIM: 102700) (8, 9). Two genetic anomalies can account for this disorder: either mutation in the recombination-activating (*RAG1* and *RAG2*) genes or in *Artemis* gene (10). There are two *RAG* genes (*RAG1* and *RAG2*), whose functions are essential for the rearrangement of antigen receptors on T and B lymphocytes. Since this rearrangement is an essential step in lymphocyte differentiation, functionally defective *RAG* proteins are at the origin of the observed absence of T and B lymphocyte populations in these patients. Other genes required for antigen-receptor rearrangement and, more generally, double-strand DNA repair are very probably responsible for the alymphomatosis form of SCID in certain patients, particularly those whose cells present enhanced sensitivity to ionizing radiation *in vitro* (11, 12). One of these genes was recently localized to chromosome 10p (13).

Methods of biological diagnosis

Study of the segregation of the disease in the familial forms and analysis of the different lymphocyte populations generally enables them to be distinguished. In the case of alymphocytosis, immunological studies demonstrate the absence of T-lymphocyte populations, both CD4⁺ and CD8⁺, and B lymphocytes, with resulting agammaglobulinemia. Natural killer (NK) cells are present (2).

In X-linked SCID (3, 4) and SCID due to janus kinase 3 (*JAK3*) anomaly (5), T lymphocytes and NK cells are absent but B cells are present in normal or higher numbers.

Normal erythrocytic ADA levels exclude this diagnosis.

Some SCID subjects have circulating T lymphocytes of maternal origin that can be detected due to mother-to-child passage during pregnancy. HLA typing of this population can determine its true origin (6).

Prenatal diagnosis

Prenatal diagnosis of this immune deficiency relies primarily on the demonstration of the absence of the different lymphocyte populations and thus their function. This diagnosis is made at

20 weeks of gestation by analysis of fetal blood. In families whose *RAG* gene mutation has been identified or for whom the genetic link of the disease to the locus present on chromosome 10p could be established, prenatal diagnosis can be made at 11 weeks of amenorrhea on a trophoblast biopsy by studying the segregation of the associated polymorphic markers or by direct detection of the mutation in the identified genes.

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