A DELETION IN THE GENE ENCODING THE CD45 ANTIGEN IN A PATIENT WITH SCID


Purpose of the Study. Defects in genes required for the development of T cells often underlie the primary immunodeficiency known as severe combined immunodeficiency (SCID). Many gene defects have been identified in SCID patients although the most common is the X-linked form of SCID that is attributable to defects in the common cytokine receptor chain. This study examined the cause of a novel type of SCID that was associated with minimal surface expression of CD45. CD45 is an abundant cell surface protein with multiple isoforms. It is a protein tyrosine phosphatase that is critical for transmembrane signal transduction.

Methods. Peripheral blood mononuclear cells from the patient were examined for expression of CD45 using standard flow cytometry techniques. The CD45 gene was sequenced using polymerase chain reaction. To confirm the role of the mutation in the defective expression of CD45, the mutant cDNA was transfected into Chinese hamster ovary cells.

Results. The patient was found to have a homozygous mutation in CD45. The 6bp deletion was located in the extracellular domain. The mutation did not affect transcript stability or translation, but protein was undetectable at the cell surface. This was true for 3 of the 8 isoforms examined and could be presumed to similarly affect all isoforms.

Conclusions. The homozygous mutation in CD45 was not found in any normal controls and was found to reproduce the defect in transfection experiments. The authors conclude that this 6bp deletion in the extracellular domain was responsible for the reduced surface expression of CD45 and the patient’s SCID.

Reviewer’s Comments. This particular patient was the first identified as being CD45-deficient in 1997, although the mutation was not identified until this manuscript. It is apparently a rare type of SCID with only 2 patients known to be CD45-deficient. This study demonstrates the importance of the 2 deleted amino acids in the surface expression of CD45 and serves as a reminder of the many types of defects that can potentially be associated with SCID.

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INTRAVenous GAMMA GLOBULIN THERAPY

ANTINFLAMMATORY ACTIVITY OF IVIG MEDIATED THROUGH THE INHIBITORY FC RECEPTOR


Purpose of the Study. High-dose intravenous gamma globulin (IVIG) has proven effective for the treatment of autoimmune diseases such as immune thrombocytopenia (ITP), but the mechanism for its beneficial effects have not been clearly defined. In this study, the molecular basis for the antiinflammatory property of IVIG was investigated in a murine model of ITP.

Methods. ITP was induced in mice through the injection of an antiplatelet monoclonal antibody (mAb), and pretreatment with either IVIG or Fc antibody fragments (which bind to Fcy receptors on cells, but cannot bind antigens) could prevent the resulting thrombocytopenia. Through the use of specific blocking antibodies and transgenic mice, the authors tested whether IgG receptors (FcyRIIB, FcγRIIB) were involved in the protective effects of IVIG.

Results. The FcγRIIB receptor was required for protection, as demonstrated by genetic deletion or blocking with mAb. In addition, protection by IVIG was associated with the induction of FcγRIIB, which inhibits macrophage acti-
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