Memory Switched B Cell Percentage and Not Serum Immunoglobulin Concentration Is Associated With Clinical Complications in Children and Adults With Specific Antibody Deficiency and Common Variable Immunodeficiency


PURPOSE OF THE STUDY. To compare the associations of clinical complications of antibody deficiency with (1) measures of memory B-cell development and (2) serum immunoglobulin (Ig) concentrations.

STUDY POPULATION. Twenty-seven children (aged 2–16 years) and 28 adults (aged 22–65 years) with diagnoses of specific antibody deficiency defined as having normal Ig levels and impaired responses to pneumococcal immunization (specific antibody deficiency [SAD], 21 patients) or common variable immunodeficiency defined as hypogammaglobulinemia with more generally impaired vaccine responses (common variable immunodeficiency [CVID]; 34 patients) were studied. Nineteen patients who underwent evaluation and were found to have normal Ig levels and fully intact vaccine responses served as a “control” group.

METHODS. Serum Ig levels were measured by standard clinical laboratory methods; memory B-cell populations were assessed by flow cytometry using labeled monoclonal antibodies to detect cell-surface CD19, CD27, and IgD. (CD19 is a marker for all B cells. CD27 is a marker for the memory subset of cells. Cells that do not express IgD have undergone class-switching and express IgG, IgA, or IgE. CD19^−CD27^−IgD^− cells are called “switched” memory B cells and are indicators of normal B-cell activation and development in germinal centers in lymph nodes or other secondary lymphoid tissues.) These laboratory findings were separately correlated with clinical characteristics.

RESULTS. The only significant laboratory differences between the SAD and CVID groups were the serum concentrations of IgG and IgA, which was expected because of the laboratory definitions of these entities. There were no differences in memory B-cell populations nor the occurrence of splenomegaly, bronchiectasis, and autoimmune disease (enteropathy, cytopenias, arthritis, diabetes) between the groups with SAD and CVID. However, when patients with each of these complications (without regard to immunodeficiency diagnosis) were compared with those without, a significantly (P < .01) lower percentage and number of switched memory B cells was found in the affected patients. The statistical significance was unchanged after adjustment for age. Serum Ig levels were not different in patients with or without each of these complications, even after adjusting for age.

CONCLUSIONS. Measurement of switched memory B cells is a more accurate predictor of clinical complications of humoral immunodeficiency than is the classification of SAD and CVID or measurement of serum Ig.

REVIEWER COMMENTS. Measurement of memory B-cell populations has emerged in the past 5 years as a potentially clinically useful predictor of complications for patients with CVID, with reports of findings similar to those in this article. This study extends this observation to another diagnosis: SAD. This study was also the first to compare children and adults with these 2 diagnoses with respect to clinical and laboratory features. Although the numbers are relatively small, neither the diagnostic assignment nor measurement of serum Ig concentration (related by the clinical/laboratory definitions of these syndromes) allows one to predict the occurrence of the complications studied. Even across diagnoses, the determination of switched memory B-cell percentage emerges as a robust indicator of associated complications. This laboratory test is likely to become a part of the routine evaluation of humoral immunodeficiency.

Infants Presenting With Recurrent Infections and Low Immunoglobulins: Characteristics and Analysis of Normalization


PURPOSE OF THE STUDY. To determine the outcomes of infants and young children with recurrent infections found to have low levels of ≥1 immunoglobulin (Ig) class (IgG, IgA, or IgM) without other screening laboratory indicators of immunodeficiency.

STUDY POPULATION. Forty-nine infants who presented for evaluation at <24 months of age and had IgG, IgA, or IgM levels of <2 SD below the age-adjusted mean, intact antibody response to tetanus and diphtheria, intact cellular immunity, and no other immunodeficiency diagnoses.

METHODS. Retrospective review of medical charts at a single institution from 1977 to 2005.

RESULTS. Boys accounted for 70% of the patients. Recurrent otitis media was the predominant presentation (78%). Significant associated features were recurrent wheezing with infection (61%) and atopy (27%). Multiple isotypes were reduced in 65% of the patients; low
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*Pediatrics* 2007;120;S156

DOI: 10.1542/peds.2007-0846

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